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(71) Applicant: DUKE UNIVERSITY [US/US]; Erwin Road, Durham, NC 27706 (US).		
(72) Inventors: BOLOGNESI, Dani, P.; 17 Harvey Place, Durham, NC 27705 (US). MATTHEWS, Thomas, J.; 5906 Newhall Road, Durham, NC 27713 (US). WILD, Carl, T.; 1702 B Vista Street, Durham, NC 27701 (US). BARNEY, Shaen, O'Lin; 106 Branchway Road, Cary, NC 27502 (US). LAMBERT, Dennis, M.; 101 Centerville Court, Cary, NC 27513 (US). PETTEWAY, Stephen, R., Jr.; 203 Le Gault Drive, Cary, NC 27513 (US).		
(74) Agents: CORUZZI, Laura, A. et al.; Pennie & Edmonds, 1155 Avenue of the Americas, New York, NY 10036 (US).		

(54) Title: SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION

(57) Abstract

The present invention relates to peptides which exhibit potent anti-retroviral activity. The peptides of the invention comprise DP-178 (SEQ ID:1) peptide corresponding to amino acids 638 to 673 of the HIV-1 LAI gp41 protein, and fragments, analogs and homologs of DP-178. The invention further relates to the uses of such peptides as inhibitory of human and non-human retroviral, especially HIV, transmission to uninfected cells.

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SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION1. INTRODUCTION

The present invention relates to DP-178 (SEQ ID:1), a peptide corresponding to amino acids 638 to 673 of the HIV-1_{LAI} transmembrane protein (TM) gp41, and portions, analogs, and homologs of DP-178 (SEQ ID:1), all of which exhibit anti-viral activity. Such anti-viral activity includes, but is not limited to, the inhibition of HIV transmission to uninfected CD-4⁺ cells. Further, the invention relates to the use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells. Still further, the invention relates to the use of DP-178 as a HIV subtype-specific diagnostic.

The present invention also relates to antiviral peptides analogous to DP-107, a peptide corresponding to amino acids 558 to 595 of the HIV-1_{LAI} transmembrane protein (TM) gp41, that are present in other enveloped viruses. The present invention further relates to methods for identifying antiviral compounds that disrupt the interaction between DP-178 and DP-107, and/or between DP-107-like and DP-178-like peptides.

The invention is demonstrated by way of a working example wherein DP-178 (SEQ ID:1), and a peptide whose sequence is homologous to DP-178 are each shown to be potent, non-cytotoxic inhibitors of HIV-1 transfer to uninfected CD-4⁺ cells. The invention is further demonstrated by working examples wherein peptides having antiviral and/or structural similarity to DP-107 and DP-178 are identified.

2. BACKGROUND OF THE INVENTION

2.1. THE HUMAN IMMUNODEFICIENCY VIRUS

The human immunodeficiency virus (HIV) has been implicated as the primary cause of the slowly degenerative immune system disease termed acquired 5 immune deficiency syndrome (AIDS) (Barre-Sinoussi, F. et al., 1983, *Science* 220:868-870; Gallo, R. et al., 1984, *Science* 224:500-503). There are at least two distinct types of HIV: HIV-1 (Barre-Sinoussi, F. et al., 1983, *Science* 220:868-870; Gallo R. et al., 1984, 10 *Science* 224:500-503) and HIV-2 (Clavel, F. et al., 1986, *Science* 233:343-346; Guyader, M. et al., 1987, *Nature* 326:662-669). Further, a large amount of 15 genetic heterogeneity exists within populations of each of these types. Infection of human CD-4⁺ T-lymphocytes with an HIV virus leads to depletion of the cell type and eventually to opportunistic infections, neurological dysfunctions, neoplastic growth, and ultimately death.

HIV is a member of the lentivirus family of 20 retroviruses (Teich, N. et al., 1984, *RNA Tumor Viruses*, Weiss, R. et al., eds., CSH-Press, pp. 949-956). Retroviruses are small enveloped viruses that contain a diploid, single-stranded RNA genome, and 25 replicate via a DNA intermediate produced by a virally-encoded reverse transcriptase, an RNA-dependent DNA polymerase (Varmus, H., 1988, *Science* 240:1427-1439). Other retroviruses include, for example, oncogenic viruses such as human T-cell leukemia viruses (HTLV-I,-II,-III), and feline 30 leukemia virus.

The HIV viral particle consists of a viral core, composed of capsid proteins, that contains the viral RNA genome and those enzymes required for early replicative events. Myristylated Gag protein forms an 35

outer viral shell around the viral core, which is, in turn, surrounded by a lipid membrane envelope derived from the infected cell membrane. The HIV envelope surface glycoproteins are synthesized as a single 160 Kd precursor protein which is cleaved by a cellular protease during viral budding into two glycoproteins, gp41 and gp120. gp41 is a transmembrane protein and gp120 is an extracellular protein which remains non-covalently associated with gp41, possibly in a trimeric or multimeric form (HammarSKJOLD, M. and REKOSH, D., 1989, *Biochem. Biophys. Acta* 989:269-280).

HIV is targeted to CD-4⁺ cells because the CD-4 cell surface protein acts as the cellular receptor for the HIV-1 virus (DALGLEISH, A. *et al.*, 1984, *Nature* 312:763-767; KLATZMANN *et al.*, 1984, *Nature* 312:767-768; MADDON *et al.*, 1986, *Cell* 47:333-348). Viral entry into cells is dependent upon gp120 binding the cellular CD-4⁺ receptor molecules (McDOUGAL, J.S. *et al.*, 1986, *Science* 231:382-385; MADDON, P.J. *et al.*, 1986, *Cell* 47:333-348) and thus explains HIV's tropism for CD-4⁺ cells, while gp41 anchors the envelope glycoprotein complex in the viral membrane.

2.2. HIV TREATMENT

HIV infection is pandemic and HIV associated diseases represent a major world health problem. Although considerable effort is being put into the successful design of effective therapeutics, currently no curative anti-retroviral drugs against AIDS exist. In attempts to develop such drugs, several stages of the HIV life cycle have been considered as targets for therapeutic intervention (MITSUYA, H. *et al.*, 1991, *FASEB J.* 5:2369-2381). For example, virally encoded reverse transcriptase has been one focus of drug development. A number of reverse-transcriptase-

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targeted drugs, including 2',3'-dideoxynucleoside analogs such as AZT, ddi, ddc, and d4T have been developed which have been shown to be active against HIV (Mitsuya, H. *et al.*, 1991, *Science* **249**:1533-1544). While beneficial, these nucleoside analogs are not 5 curative, probably due to the rapid appearance of drug resistant HIV mutants (Lander, B. *et al.*, 1989, *Science* **243**:1731-1734). In addition, the drugs often exhibit toxic side effects such as bone marrow suppression, vomiting, and liver function 10 abnormalities.

Attempts are also being made to develop drugs which can inhibit viral entry into the cell, the earliest stage of HIV infection. Here, the focus has thus far been on CD4, the cell surface receptor for 15 HIV. Recombinant soluble CD4, for example, has been shown to inhibit infection of CD-4⁺ T-cells by some HIV-1 strains (Smith, D.H. *et al.*, 1987, *Science* **238**:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition 20 by recombinant CD-4 (Daar, E. *et al.*, 1990, *Proc. Natl. Acad. Sci. USA* **87**:6574-6579). In addition, recombinant soluble CD-4 clinical trials have produced inconclusive results (Schooley, R. *et al.*, 1990, *Ann. 25 Int. Med.* **112**:247-253; Kahn, J.O. *et al.*, 1990, *Ann. Int. Med.* **112**:254-261; Yarchoan, R. *et al.*, 1989, *Proc. Vth Int. Conf. on AIDS*, p. 564, MCP 137).

The late stages of HIV replication, which involve crucial virus-specific secondary processing of certain viral proteins, have also been suggested as possible 30 anti-HIV drug targets. Late stage processing is dependent on the activity of a viral protease, and drugs are being developed which inhibit this protease (Erickson, J., 1990, *Science* **249**:527-533). The

clinical outcome of these candidate drugs is still in question.

Attention is also being given to the development of vaccines for the treatment of HIV infection. The HIV-1 envelope proteins (gp160, gp120, gp41) have been shown to be the major antigens for anti-HIV antibodies present in AIDS patients (Barin, *et al.*, 1985, *Science* 228:1094-1096). Thus far, therefore, these proteins seem to be the most promising candidates to act as antigens for anti-HIV vaccine development. To this end, several groups have begun to use various portions of gp160, gp120, and/or gp41 as immunogenic targets for the host immune system. See for example, Ivanoff, L. *et al.*, U.S. Pat. No. 5,141,867; Saith, G. *et al.*, WO 92/22,654; Shafferman, A., WO 91/09,872; Formoso, C. *et al.*, WO 90/07,119. Clinical results concerning these candidate vaccines, however, still remain far in the future.

Thus, although a great deal of effort is being directed to the design and testing of anti-retroviral drugs, a truly effective, non-toxic treatment is still needed.

3. SUMMARY OF THE INVENTION

The present invention relates to DP-178 (SEQ ID:1), a 36-amino acid synthetic peptide corresponding to amino acids 638 to 673 of the transmembrane protein (TM) gp41 from the HIV-1 isolate LAI, which exhibits potent anti-HIV-1 activity. As evidenced by the example presented below, in Section 6, the DP-178 (SEQ ID:1) anti-viral activity is so high that, on a weight basis, no other known anti-HIV agent is effective at concentrations as low as those at which DP-178 (SEQ ID:1) exhibits its inhibitory effects. The invention further relates to those portions, analogs, and

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homologs of DP-178 which also show such antiviral activity. The antiviral activity of such DP-178 portions, analogs, and homologs, includes, but is not limited to the inhibition of HIV transmission to uninfected CD-4⁺ cells. The invention relates to the
5 use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs. Such uses may include, but are not limited to, the use of the peptides as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells, and as type and/or
10 subtype-specific diagnostic tools.

An embodiment of the invention is demonstrated below wherein an extremely low concentration of DP-178 (SEQ ID:1), and very low concentrations of a DP-178 homolog (SEQ ID:3) are shown to be potent inhibitors
15 of HIV-1 mediated CD-4⁺ cell-cell fusion (*i.e.*, syncytial formation) and infection of CD-4⁺ cells by cell-free virus. Further, it is shown that DP-178 (SEQ ID:1) is not toxic to cells, even at concentrations 3 logs higher than the inhibitory
20 DP-178 (SEQ ID:1) concentration.

The invention also relates to analogous DP178 peptides in other enveloped viruses that demonstrate similar antiviral properties.

The invention further relates to peptides
25 analogous to DP-107, a peptide corresponding to amino acids 558-595 of the HIV-1_{LAI} transmembrane protein (TM) of gp41, that are present in other enveloped viruses, and demonstrate antiviral properties. The present invention is based, in part, on the surprising
30 discovery that the DP-107 and DP-108 domains of the gp41 protein non-covalently complex with each other, and that their interaction is necessary for the normal activity of the virus. The invention, therefore,
35 further relates to methods for identifying antiviral

compounds that disrupt the interaction between DP-107 and DP-178, and/or between DP-107-like and DP-178-like peptides.

Embodiments of the invention are demonstrated, below, wherein peptides having structural and/or 5 similarity to DP-107 and DP-178 are identified.

3.1. DEFINITIONS

Peptides are defined herein as organic compounds comprising two or more amino acids covalently joined 10 by peptide bonds. Peptides may be referred to with respect to the number of constituent amino acids, i.e., a dipeptide contains two amino acid residues, a tripeptide contains three, etc. Peptides containing ten or fewer amino acids may be referred to as 15 oligopeptides, while those with more than ten amino acid residues are polypeptides.

Peptide sequences defined herein are represented by one-letter symbols for amino acid residues as follows:

- 20 A (alanine)
- R (arginine)
- N (asparagine)
- D (aspartic acid)
- C (cysteine)
- 25 Q (glutamine)
- E (glutamic acid)
- G (glycine)
- H (histidine)
- I (isoleucine)
- 30 L (leucine)
- K (lysine)
- M (methionine)
- F (phenylalanine)
- P (proline)

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S (serine)
T (threonine)
W (tryptophan)
Y (tyrosine)
V (valine)

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4. BRIEF DESCRIPTION OF THE FIGURES

FIG. 1. Amino acid sequence of DP-178 (SEQ ID:1) derived from HIV_{LAI}; DP-178 homologs derived from HIV-1_{SP2} (DP-185; SEQ ID:3), HIV-1_{RF} (SEQ ID:4), and HIV-1_{MN} (SEQ ID:5); DP-178 homologs derived from amino acid sequences of two prototypic HIV-2 isolates, namely, HIV-2_{rod} (SEQ ID:6) and HIV-2_{NHZ} (SEQ ID:7); control peptides: DP-180 (SEQ ID:2), a peptide incorporating the amino acid residues of DP-178 in a scrambled sequence; DP-118 (SEQ ID:10) unrelated to DP-178, which inhibits HIV-1 cell free virus infection; DP-125 (SEQ ID:8), unrelated to DP-178, was also previously shown to inhibit HIV-1 cell free virus infection (Wild *et al.*, 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541); DP-116 (SEQ ID:9), unrelated to DP-178 had previously been shown to be negative for inhibition of HIV-1 infection using the cell-free virus infection assay (Wild, *et al.*, 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541). Throughout the figures, the one letter amino acid code is used.

FIG. 2. Inhibition of HIV-1 cell-free virus infection by synthetic peptides. IC50 refers to the concentration of peptide that inhibits RT production from infected cells by 50% compared to the untreated control. Control: the level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

FIG. 3. Inhibition of HIV-1 and HIV-2 cell-free virus infection by the synthetic peptide DP-178 (SEQ

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ID:1). IC50: concentration of peptide that inhibits RT production by 50% compared to the untreated control. Control: Level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

5 FIG. 4A. Fusion Inhibition Assay. DP-178 (SEQ ID:1) inhibition of HIV-1 prototypic isolate-mediated syncytia formation. Data represents the number of virus-induced syncytia per cell.

10 FIG. 4B. Fusion Inhibition Assay. DP-180 (SEQ ID:2): scrambled control peptide. DP-185 (SEQ ID:3): DP-178 homolog derived from HIV-1_{SP2} isolate. Control: number of syncytia produced in the absence of peptide.

15 FIG. 5. Fusion inhibition assay: HIV-1 vs. HIV-2. Data represents the number of virus-induced syncytia per well. ND: not done.

FIG. 6. Cytotoxicity study of DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9) on CEM cells. Cell proliferation data is shown.

20 FIG. 7. Schematic representation of HIV-gp41 and maltose binding protein (MBP)-gp41 fusion proteins. DP107 and DP178 are synthetic peptides based on the two putative helices of gp41. The letter P in the DP107 boxes denotes an Ile to Pro mutation at amino acid number 578. Amino acid residues are numbered according to Meyers et al., Human Retroviruses and AIDS, 1991, Theoret. Biol. and Biophys. Group, Los Alamos Natl. Lab., Los Alamos, NM.

25 FIG. 8. A point mutation alters the conformation and anti-HIV activity of M41.

30 FIG. 9. Abrogation of DP178 anti-HIV activity. Cell fusion assays were carried out in the presence of 10 nM DP178 and various concentrations of M41Δ178 or M41PΔ178.

FIG. 10. Binding of DP178 to leucine zipper of gp41 analyzed by ELISA.

FIG. 11A-B. Models for a structural transition in the HIV-1 TM protein. Two models are proposed which indicate a structural transition from a native oligomer to a fusogenic state following a trigger event (possibly gp120 binding to CD4). Common features of both models include (1) the native state is held together by noncovalent protein-protein interactions to form the heterodimer of gp120/41 and other interactions, principally through gp41 interactive sites, to form homo-oligomers on the virus surface of the gp120/41 complexes; (2) shielding of the hydrophobic fusogenic peptide at the N-terminus (F) in the native state; and (3) the leucine zipper domain (DP107) exists as a homo-oligomer coiled coil only in the fusogenic state. The major differences in the two models include the structural state (native or fusogenic) in which the DP107 and DP178 domains are complexed to each other. In the first model (A; FIG. 11A) this interaction occurs in the native state and in B during the fusogenic state. When triggered, the fusion complex in the model depicted in (A) is generated through formation of coiled-coil interactions in homologous DP107 domains resulting in an extended α -helix. This conformational change positions the fusion peptide for interaction with the cell membrane. In the second model (B; FIG. 11B), the fusogenic complex is stabilized by the association of the DP178 domain with the DP107 coiled-coil.

FIG. 12. Motif design using heptad repeat positioning of amino acids of known coiled-coils.

FIG. 13. Motif design using proposed heptad repeat positioning of amino acids of DP-107 and DP-178.

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FIG. 14. Hybrid motif design crossing GCN4 and DP-107.

FIG. 15. Hybrid motif design crossing GCN4 and DP-178.

5 FIG. 16. Hybrid motif design 107x178x4, crossing DP-107 and DP-178. This motif was found to be the most consistent at identifying relevant DP-107-like and DP-178-like peptide regions.

FIG. 17. Hybrid motif design ALLMOTI5, crossing GCN4, DP-107, and DP-178.

10 FIG. 18. Hybrid motif design crossing GCN4, DP-107, DP-178, c-Fos c-Jun, c-Myc, and Flu Loop 36.

FIG. 19. Motifs designed to identify N-terminal proline-leucine zipper motifs.

15 FIG. 20. Search results for HIV-1 (BRU isolate) envelope protein gp41. Sequence search motif designations: Spades (♦): 107x178x4; Hearts (♥) ALLMOTI5; Clubs (♣): PLZIP; Diamonds (♦): transmembrane region (the putative transmembrane domains were identified using a PC/Gene program 20 designed to search for such peptide regions).

Asterisk (*): Lupas method. The amino acid sequences identified by each motif are bracketed by the respective characters. Representative sequences chosen based on all searches are underlined and in bold. DP-107 and DP-178 sequences are marked, and 25 additionally double-underlined and italicized.

FIG. 21. Search results for human respiratory syncytial virus (RSV) strain A2 fusion glycoprotein F1. Sequence search motif designations 30 are as in FIG. 20.

FIG. 22. Search results for simian immunodeficiency virus (SIV) envelope protein gp41 (AGM3 isolate). Sequence search motif designations are as in FIG. 20.

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FIG. 23. Search results for canine distemper virus (strain Onderstepoort) fusion glycoprotein 1. Sequence search motif designations are as in FIG. 20.

5 FIG. 24. Search results for newcastle disease virus (strain Australia-Victoria/32) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

10 FIG. 25. Search results for human parainfluenza 3 virus (strain NIH 47885) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

15 FIG. 26. Search results for influenza A virus (strain A/AICHI/2/68) hemagglutinin precursor HA2. Sequence search designations are as in FIG. 20.

20 FIG. 27. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 48-amino acid RSV F2 peptide which spans sequences identified utilizing the computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 21. "+" symbols are relative indicators of either structural similarity or antiviral activity, with a greater number of "+" symbols indicating a higher relative similarity or antiviral activity.

25 FIG. 28. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 53-amino acid RSV F1 peptide which spans sequences identified utilizing the computer-assisted searches described herein. See FIG. 21 for the exact location and motifs used. "+" symbols are as described for FIG. 27.

30 FIG. 29. Coiled-coil structural similarity and anti-human parainfluenza 3 virus (HPF3) antiviral activity of 35-mer peptides synthesized utilizing the

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sequence of a 56-amino acid HPF3 peptide which spans sequences identified utilizing computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

5 FIG. 30. Coiled-coil structural similarity and anti-HPF3 antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 70-amino acid HPF3 peptide which spans sequences identified utilizing the computer-assisted searches described
10 herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

5. DETAILED DESCRIPTION OF THE INVENTION

15 Described herein are peptides that exhibit potent antiviral activity. These peptides include DP-178 (SEQ ID:1), a gp41-derived 36 amino acid peptide, fragments and/or analogs of DP-178, and peptides which are homologous to DP-178. In addition, these peptides may include peptides exhibiting anti-viral activity
20 which are analogous to DP-107, a 38 amino acid peptide corresponding to residues 558 to 595 of the HIV-1_{LA1} transmembrane (TM) gp41 protein, and which are present in other enveloped viral proteins. Also described
25 here are assays for testing the antiviral activities of such peptides. The present invention is based, in part, of the surprising discovery that the DP-107 and DP-178 domains of the gp41 protein complex with each other via non-covalent protein-protein interactions which are necessary for normal activity of the virus.
30 As such, methods are described for the identification of antiviral compounds that disrupt the interaction between DP-107 and DP-178 peptides, and between DP-107-like and DP-178-like peptides. Finally, the use
35 of the peptides of the invention as inhibitors of non-

human and human viral and retroviral, esp cially HIV, transmission are detailed, as is the use of the peptides as diagnostic indicators of the presence of specific, viruses, especially retroviruses.

While not limited to any theory of operation, the
5 following model is proposed to explain the potent
anti-HIV activity of DP178, based, in part, on the
experiments described in the working examples, infra.
In the viral protein, gp41, DP178 corresponds to a
10 putative α -helix region located in the C-terminal end
of the gp41 ectodomain, and appears to associate with
a distal site on gp41 whose interactive structure is
influenced by the leucine zipper motif, a coiled-coil
structure, referred to as DP107. The association of
15 these two domains may reflect a molecular linkage or
"molecular clasp" intimately involved in the fusion
process. It is of interest that mutations in the
C-terminal α -helix motif of gp41 (*i.e.*, the D178
domain) tend to enhance the fusion ability of gp41,
whereas mutations in the leucine zipper region (*i.e.*,
20 the DP107 domain) decrease or abolish the fusion
ability of the viral protein. It may be that the
leucine zipper motif is involved in membrane fusion
while the C-terminal α -helix motif serves as a
molecular safety to regulate the availability of the
25 leucine zipper during virus-induced membrane fusion.

On the basis of the foregoing, two models are
proposed of gp41-mediated membrane fusion which are
schematically shown in FIG. 11A-B. The reason for
proposing two models is that the temporal nature of
30 the interaction between the regions defined by DP107
and DP178 cannot, as yet, be pinpointed. Each model
envisiones two conformations for gp41 - one in a
"native" state as it might be found on a resting
virion. The other in a "fusogenic" state to reflect
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conformational change is triggered following binding of gp120 to CD4 and just prior to fusion with the target cell membrane. The strong binding affinity between gp120 and CD4 may actually represent the trigger for the fusion process obviating the need for a pH change such as occurs for viruses that fuse within intracellular vesicles. The two major features of both models are: (1) the leucine zipper sequences (DP107) in each chain of oligomeric envelope are held apart in the native state and are only allowed access to one another in the fusogenic state so as to form the extremely stable coiled-coils, and (2) association of the DP178 and DP107 sites as they exist in gp41 occur either in the native or fusogenic state. FIG. 11A depicts DP178/DP107 interaction in the native state as a molecular class. On the other hand, if one assumes that the most stable form of the envelope occurs in the fusogenic state, the model in FIG. 11B can be considered.

When synthesized as peptides, both DP107 and DP178 are potent inhibitors of HIV infection and fusion, probably by virtue of their ability to form complexes with viral gp41 and interfere with its fusogenic process; e.g., during the structural transition of the viral protein from the native structure to the fusogenic state, the DP178 and DP107 peptides may gain access to their respective binding sites on the viral gp41, and exert a disruptive influence. DP107 peptides which demonstrate anti-HIV activity are described in Applicants' co-pending application Serial No. 07/927,532, filed August 7, 1992, which is incorporated by reference herein in its entirety.

As shown in the working examples, infra, a truncated recombinant gp41 protein corresponding the

ectodomain of gp41 containing both DP107 and DP178 domains (excluding the fusion peptide, transmembrane region and cytoplasmic domain of gp41) did not inhibit HIV-1 induced fusion. However, when a single mutation was introduced to disrupt the coiled-coil structure of 5 the DP107 domain -- a mutation which results in a total loss of biological activity of DP107 peptides -- the inactive recombinant protein was transformed to an active inhibitor of HIV-1 induced fusion. This transformation may result from liberation of the 10 potent DP178 domain from a molecular clasp with the leucine zipper, DP107 domain.

For clarity of discussion, the invention will be described for DP178 peptide inhibitors of HIV. 15 However, the principles may be analogously applied to other fusogenic enveloped viruses, including but not limited to those viruses containing the peptides listed in Tables V through X, below.

5.1. DP-178 AND DP-178-LIKE PEPTIDES

20 The peptide DP-178 (SEQ ID:1) of the invention corresponds to amino acid residues 638 to 673 of the transmembrane protein gp41 from the HIV-1_{LAI} isolate, and has the 36 amino acid sequence (reading from amino to carboxy terminus):

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NH₂-YTSLIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:1)

In addition to the full-length DP-178 (SEQ ID:1) 36-mer, the peptides of the invention may include 30 truncations of the DP-178 (SEQ ID:1) peptide which exhibit antiviral activity. Such truncated DP-178 (SEQ ID:1) peptides may comprise peptides of between 3 and 36 amino acid residues (*i.e.*, peptides ranging in size from a tripeptide to a 36-mer polypeptide), and 35

may include but are not limited to those listed in Tables I and II, below. Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group (-NH₂) and "Z" may represent a carboxyl (-COOH) group.

- 5 Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a FMOC group, an amido group, or a covalently attached macromolecule.

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TABLE I
DP-178 (SEQ ID:1) CARBOXY TRUNCATIONS

X-YTS-Z
 X-YTSL-Z
 X-YTSLI-Z
 X-YTSLIH-Z
 5 X-YTSLIHS-Z
 X-YTSLIHSL-Z
 X-YTSLIHSLI-Z
 X-YTSLIHSLIE-Z
 X-YTSLIHSLIEE-Z
 X-YTSLIHSLIEES-Z
 X-YTSLIHSLIEESQ-Z
 10 X-YTSLIHSLIEESQN-Z
 X-YTSLIHSLIEESQNQ-Z
 X-YTSLIHSLIEESQNQQ-Z
 X-YTSLIHSLIEESQNQQE-Z
 X-YTSLIHSLIEESQNQQEK-Z
 X-YTSLIHSLIEESQNQQEKN-Z
 X-YTSLIHSLIEESQNQQEKNE-Z
 X-YTSLIHSLIEESQNQQEKNEQ-Z
 15 X-YTSLIHSLIEESQNQQEKNEQE-Z
 X-YTSLIHSLIEESQNQQEKNEQEL-Z
 X-YTSLIHSLIEESQNQQEKNEQELL-Z
 X-YTSLIHSLIEESQNQQEKNEQELLE-Z
 X-YTSLIHSLIEESQNQQEKNEQELLED-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDK-Z
 20 X-YTSLIHSLIEESQNQQEKNEQELLELDKW-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWA-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWAS-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWASL-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLW-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWN-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNW-Z
 X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z

25 The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group,
 including but not limited to carbobenzoyl, dansyl, or
 30 T-butyloxycarbonyl; an acetyl group; a 9-
 fluorenylmethoxy-carbonyl (Fmoc) group; a
 macromolecular carrier group including but not limited
 to lipid-fatty acid conjugates, polyethylene glycol,
 or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a
 T-butyloxycarbonyl group; a macromolecular carrier
 35 group including but not limited to lipid-fatty acid
 conjugates, polyethylene glycol, or carbohydrates.

TABLE II
DP-178 (SEQ ID:1) AMINO TRUNCATIONS

5	X-NWF-Z X-WNWF-Z X-LWNWF-Z X-SLWNWF-Z X-ASLWNWF-Z X-WASLWNWF-Z X-KWASLWNWF-Z X-DKWASLWNWF-Z X-LDKWASLWNWF-Z X-ELDKWASLWNWF-Z X-LELDKWASLWNWF-Z X-LLELDKWASLWNWF-Z X-ELLELDKWASLWNWF-Z X-QELLELDKWASLWNWF-Z X-EQELLELDKWASLWNWF-Z X-NEQELLELDKWASLWNWF-Z X-KNEQELLELDKWASLWNWF-Z X-EKNEQELLELDKWASLWNWF-Z X-QEKNEQELLELDKWASLWNWF-Z X-QQEKNQNEQELLELDKWASLWNWF-Z X-NQQEKNEQELLELDKWASLWNWF-Z X-QNQQEKNEQELLELDKWASLWNWF-Z X-SQNQQEKNEQELLELDKWASLWNWF-Z X-ESQNQQEKNEQELLELDKWASLWNWF-Z X-EESQNQQEKNEQELLELDKWASLWNWF-Z X-IEESQNQQEKNEQELLELDKWASLWNWF-Z X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z X-LIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z X-SLIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z X-TSLIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z X-YTSIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z
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25	The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoxy, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

The antiviral peptides of the invention also include analogs of DP-178 and/or DP-178 truncations which may include, but are not limited to, peptides comprising the DP-178 (SEQ ID:1) sequence, or DP-178 truncated sequence, containing one or more amino acid 5 substitutions, insertions and/or deletions. Analogs of DP-178 homologs, described below, are also within the scope of the invention. The DP-178 analogs of the invention exhibit antiviral activity, and may, further, possess additional advantageous features, 10 such as, for example, increased bioavailability, and/or stability, or reduced host immune recognition.

HIV-1 and HIV-2 envelope proteins are structurally distinct, but there exists a striking amino acid conservation within the DP-178- 15 corresponding regions of HIV-1 and HIV-2. The amino acid conservation is of a periodic nature, suggesting some conservation of structure and/or function. Therefore, one possible class of amino acid 20 substitutions would include those amino acid changes which are predicted to stabilize the structure of the DP-178 peptides of the invention.

Amino acid substitutions may be of a conserved or non-conserved nature. Conserved amino acid 25 substitutions consist of replacing one or more amino acids of the DP-178 (SEQ ID:1) peptide sequence with amino acids of similar charge, size, and/or hydrophobicity characteristics, such as, for example, a glutamic acid (E) to aspartic acid (D) amino acid substitution. When only conserved substitutions are 30 made, the resulting peptide is functionally equivalent to DP-178 (SEQ ID:1) or the DP-178 peptide from which it is derived. Non-conserved substitutions consist of replacing one or more amino acids of the DP-178 (SEQ 35 ID:1) peptide sequence with amino acids possessing dissimilar charge, size, and/or hydrophobicity

characteristics, such as, for example, a glutamic acid (E) to valine (V) substitution.

Amino acid insertions may consist of single amino acid residues or stretches of residues ranging from 2 to 15 amino acids in length. One or more insertions 5 may be introduced into DP-178 (SEQ ID:1), DP-178 fragments, analogs and/or DP-178 homologs (described below).

Deletions of DP-178 (SEQ ID:1), DP-178 fragments, 10 analogs, and/or DP-178 homologs (described below) are also within the scope of the invention. Such deletions consist of the removal of one or more amino acids from the DP-178 or DP-178-like peptide sequence, with the lower limit length of the resulting peptide sequence being 4 to 6 amino acids. Such deletions may 15 involve a single contiguous or greater than one discrete portion of the peptide sequences.

The peptides of the invention may further include homologs of DP-178 (SEQ ID:1) and/or DP-178 truncations which exhibit antiviral activity. Such 20 DP-178 homologs are peptides whose amino acid sequences are comprised of the amino acid sequences of peptide regions of other (*i.e.*, other than HIV-1_{LAI}) viruses that correspond to the gp41 peptide region from which DP-178 (SEQ ID:1) was derived. Such 25 viruses may include, but are not limited to, other HIV-1 isolates and HIV-2 isolates. DP-178 homologs derived from the corresponding gp41 peptide region of other (*i.e.*, non HIV-1_{LAI}) HIV-1 isolates may include, for example, peptide sequences as shown below.

30 NH₂-YTNTIYTLLEESQNQQEKNEQELLELDKWASLWNWF-COOH (DP-185; SEQ ID:3);

35 NH₂-YTGIYNLLEESQNQQEKNEQELLELDKWANLWNWF-COOH (SEQ ID:4);

NH₂-YTS~~L~~IY~~S~~LLEKSQIQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:5).

SEQ ID:3 (DP-185), SEQ ID:4, and SEQ ID:5 are derived from HIV-1_{SP2}, HIV-1_{RF}, and HIV-1_{MN} isolates, respectively. Underlined amino acid residues refer to those residues that differ from the corresponding position in the DP-178 (SEQ ID:1) peptide. One such DP-178 homolog, DP-185 (SEQ ID:3), is described in the Working Example presented in Section 6, below, where it is demonstrated that DP-185 (SEQ ID:3) exhibits antiviral activity. The DP-178 homologs of the invention may also include truncations, amino acid substitutions, insertions, and/or deletions, as described above.

In addition, striking similarities, as shown in FIG. 1, exist within the regions of HIV-1 and HIV-2 isolates which correspond to the DP-178 sequence. A DP-178 homolog derived from the HIV-2_{NHZ} isolate has the 36 amino acid sequence (reading from amino to carboxy terminus):

NH₂-LEANISQSLEQAQIQQEKNM~~Y~~ELQKLNSWDVFTNW~~L~~-COOH (SEQ ID:7)

Table III and Table IV show some possible truncations of the HIV-2_{NHZ} DP-178 homolog, which may comprise peptides of between 3 and 36 amino acid residues (i.e., peptides ranging in size from a tripeptide to a 36-mer polypeptide). Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group (-NH₂) and "Z" may represent a carboxyl (-COOH) group. Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a FMOC group, an amido group, or a covalently attached macromolecule, as described below.

35

TABLE III
HIV-2_{NH2} DP-178 homolog carboxy truncations.

X-LEA-Z	
X-LEAN-Z	
X-LEANI-Z	
X-LEANIS-Z	
5 X-LEANISQ-Z	
X-LEANISQS-Z	
X-LEANISQSL-Z	
X-LEANISQSLE-Z	
X-LEANISQSLEQ-Z	
X-LEANISQSLEQA-Z	
X-LEANISQSLEQAQ-Z	
10 X-LEANISQSLEQAQI-Z	
X-LEANISQSLEQAQIQ-Z	
X-LEANISQSLEQAQIQQ-Z	
X-LEANISQSLEQAQIQQE-Z	
X-LEANISQSLEQAQIQQEK-Z	
X-LEANISQSLEQAQIQQEKN-Z	
X-LEANISQSLEQAQIQQEKNM-Z	
X-LEANISQSLEQAQIQQEKNMY-Z	
15 X-LEANISQSLEQAQIQQEKNMYE-Z	
X-LEANISQSLEQAQIQQEKNMYEL-Z	
X-LEANISQSLEQAQIQQEKNMYELQ-Z	
X-LEANISQSLEQAQIQQEKNMYELQK-Z	
X-LEANISQSLEQAQIQQEKNMYELQKL-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLN-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSN-Z	
20 X-LEANISQSLEQAQIQQEKNMYELQKLSW-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWD-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDV-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDVF-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDVFT-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDVFTN-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDVFTNW-Z	
X-LEANISQSLEQAQIQQEKNMYELQKLSWDVFTNWL-Z	

25 The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoyl, dansyl, or
 30 T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

TABLE IV
HIV-2_{NH2} DP-178 homolog amino truncations.

5	X-NWL-Z X-TNWL-Z X-FTNWL-Z X-VFTNWL-Z X-DVFTNWL-Z X-WDVFTNWL-Z X-SWDVFTNWL-Z X-NSWDVFTNWL-Z X-LNSWDVFTNWL-Z X-KLNSWDVFTNWL-Z X-QKLNSWDVFTNWL-Z X-LQKLNSWDVFTNWL-Z X-ELQKLNSWDVFTNWL-Z X-YELQKLNSWDVFTNWL-Z X-MYELQKLNSWDVFTNWL-Z X-NMYELQKLNSWDVFTNWL-Z X-KNMYELQKLNSWDVFTNWL-Z X-EKNMYELQKLNSWDVFTNWL-Z X-QEKNMYELQKLNSWDVFTNWL-Z X-QQEKNMYELQKLNSWDVFTNWL-Z X-IQQEKNMYELQKLNSWDVFTNWL-Z X-QIQQEKNMYELQKLNSWDVFTNWL-Z X-AQIQQEKNMYELQKLNSWDVFTNWL-Z X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-QSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
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The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoyl, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

5.2. DP-107 and DP-178 ANALOGOUS
ANTIVIRAL PEPTIDES

Peptid sequences functionally corresponding, and thus analogous to, the DP-178 sequences of the invention, described, above, in Section 5.1 may be found in other, non-HIV-1 envelope viruses. Further, peptide sequences functionally corresponding, and thus analogous to, DP-107, an HIV-1-derived antiviral peptide, may also be found in other, non-HIV-1 envelope viruses. DP-107 is a 38 amino acid peptide corresponding to residues 558 to 595 of HIV-1_{LAI} transmembrane (TM) gp41 protein, which exhibits potent anti-viral activity. DP-107 is more fully described in Applicant's co-pending U.S. Patent Application Ser. No. 07/927,532. These DP-107-like and DP-178-like analogous peptides are present in TM proteins of envelope viruses and preferably exhibit antiviral activity, most preferably antiviral activity which is specific to the virus in which their native sequences are found.

DP-107-like and DP-178-like peptides may be identified, for example, by utilizing a computer-assisted search strategy such as that described and demonstrated, below, in the Examples presented in Sections 9 through 16. The search strategy identifies regions in other viruses that are similar in predicted secondary structure to DP-107 and DP-178.

This search strategy is described fully, below, in the Example presented in Section 9. While this search strategy is based, in part, on a primary amino acid motif deduced from DP-107 and DP-178, it is not based solely on searching for primary amino acid sequence homologies, as such protein sequence homologies exist within, but not between major groups of viruses. For example, primary amino acid sequence homology is high within the TM protein of different

strains of HIV-1 or within the TM protein of different isolates of simian immunodeficiency virus (SIV).

Primary amino acid sequence homology between HIV-1 and SIV, however, is low enough so as not to be useful.

It is not possible, therefore, to find DP-107 or DP-

5 178-like peptides within other viruses, whether structurally, or otherwise, based on primary sequence homology, alone.

Further, while it would be potentially useful to identify primary sequence arrangements of amino acids 10 based on the physical chemical characteristics of different classes of amino acids rather than based on the specific amino acids themselves, for instance, a by concentrating on the coiled-coil nature of the peptide sequence, a computer algorithm designed by 15 Lupas et al. to identify such coiled-coil propensities of regions within proteins (Lupas, A., et al., 1991 Science 252:1162-1164) is inadequate for identifying protein regions analogous to DP-107 or DP-178.

Specifically, analysis of HIV-1 gp160 (containing 20 both gp120 and gp41) using the Lupas algorithm does not identify the coiled-coil region within DP-107. It does, however, identify a region within DP-178 beginning eight amino acids N-terminal to the start of DP-178 and ending eight amino acids from the C- 25 terminus. The DP-107 peptide has been shown experimentally to form a stable coiled coil. A search based on the Lupas search algorithm, therefore, would not have identified the DP-107 coiled-coil region.

Conversely, the Lupas algorithm identified the DP-178 30 region as a potential coiled-coil motif. However, the peptide DP-178 derived from this region failed to form a coiled coil in solution. A possible explanation for the inability of the Lupas search algorithm to accurately identify coiled-coil sequences within the 35 HIV-1 TM, is that the Lupas algorithm is based on the

structure of coiled coils from proteins that are not structurally or functionally similar to the TM proteins of viruses, antiviral peptides (e.g. DP-107 and DP-178) of which are an object of this invention.

5 The computer search strategy of the invention, as demonstrated in the Examples presented below, in Sections 9 through 16, successfully identifies regions of viral TM proteins similar to DP-107 or DP-178. This search strategy was designed to be used with a commercially-available sequence database packages, 10 preferably PC/Gene. A series of motifs were designed and engineered to range in stringency from very strict to very broad, as discussed in Section 9.

15 Among the protein sequence search motifs which may be utilized in such a computer-assisted DP-107-like and DP-178-like antiviral peptide search are the 107x178x4 motif, the ALLMOTI5 motif, and the PLZIP series of motifs, each of which is described in the Example presented in Section 9, below, with 107x178x4 being preferred.

20 Coiled-coiled sequences are thought to consist of heptad amino acid repeats. For ease of description, the amino acid positions within the heptad repeats are sometimes referred to as A through G, with the first position being A, the second B, etc. The motifs used 25 to identify DP-107-like and DP-178-like sequences herein are designed to specifically search for and identify such heptad repeats. In the descriptions of each of the motifs described, below, amino acids enclosed by brackets, i.e., [], designate the only 30 amino acid residues that are acceptable at the given position, while amino acids enclosed by braces, i.e., {}, designate the only amino acids which are unacceptable at the given heptad position. When a set of bracketed or braced amino acids is followed by a 35 number in parentheses i.e., (), it refers to the

number of subsequent amino acid positions for which the designated set of amino acids hold, e.g., a (2) means "for the next two heptad amino acid positions.

The ALLMOTI5 is written as follows:

{CDGHP}-{CFP}(2)-{CDGHP}-{CFP}(3)-
 {CDGHP}-{CFP}(2)-{CDGHP}-{CFP}(3)-
 {CDGHP}-{CFP}(2)-{CDGHP}-{CFP}(3)-
 {CDGHP}-{CFP}(2)-{CDGHP}-{CFP}(3)-
 {CDGHP}-{CFP}(2)-{CDGHP}-{CFP}(3)-

Translating this motif, it would read: "at the first (A) position of the heptad, any amino acid residue except C, D, G, H, or P is acceptable, at the next two (B,C) amino acid positions, any amino acid residue except C, F, or P is acceptable, at the fourth heptad position (D), any amino acid residue except C, D, G, H, or P is acceptable, at the next three (E, F, G) amino acid positions, any amino acid residue except C, F, or P is acceptable. This motif is designed to search for five consecutive heptad repeats (thus the repeat of the first line five times), meaning that it searches for 35-mer sized peptides. It may also be designed to search for 28-mers, by only repeating the initial motif four times. With respect to the ALLMOTI5 motif, a 35-mer search is preferred. Those viral sequences identified via such an ALLMOTI5 motif are listed in Table V, below, at the end of this section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the identification of antiviral compounds, and are intended to be within the scope of the invention.

The 107x178x4 motif is written as follows:

[EFIGLNQSTVWY]-{CFMP}(2)-[EFIGLNQSTVWY]-{CFMP}(3)-
 [EFIGLNQSTVWY]-{CFMP}(2)-[EFIGLNQSTVWY]-{CFMP}(3)-
 [EFIGLNQSTVWY]-{CFMP}(2)-[EFIGLNQSTVWY]-{CFMP}(3)-
 [EFIGLNQSTVWY]-{CFMP}(2)-[EFIGLNQSTVWY]-{CFMP}(3)-

Translating this motif, it would read: "at the first (A) position of the heptad, any amino acid residue except E, F, I, K, L, N, Q, S, T, V, W, or Y

is acceptable, at the next two (B,C) amino acid positions, any amin acid residue except C, F, M or P is accepatable, at the fourth position (D), any amin acid residue except E, F, I, K, L, N, Q, S, T, V, W, or Y is acceptable, at the next three (E, F, G) amino acid positions, any amino acid residue except C, F, M or P is acceptable. This motif is designed to search for four consecutive heptad repeats (thus the repeat of the first line four times), meaning that it searches for 28-mer sized peptides. It may also be 10 designed to search for 35-mers, by repeating the initial motif five times. With respect to the 107x178x4 motif, a 28-mer search is preferred. Those viral sequences identified via such a 107x178x4 motif are listed in Table V, below, at the end of this 15 Section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the the identification of antiviral compounds, and are intended to be within the scope of the invention.

The PLZIP series of motifs are as listed in FIG. 19. These motifs are designed to identify leucine zipper coiled-coil like heptads wherein at least one proline residue is present at some predefined distance N-terminal to the repeat. These PLZIP motifs find regions of proteins with similarities to HIV-1 DP-178 25 generally located just N-terminal to the transmembrane anchor. These motifs may be translated according to the same convention described above. Each line depicted in FIG. 19 represents a single, complete search motif. "X" in these motifs refers to any amino acid residue. In instances wherein a motif contains 30 two numbers within parentheses, this refers to a variable number of amino acid residues. For example, X (1,12) is translated to "the next one to twelve amino acid residues, inclusive, may be any amino acid".

Tables VI through X, below, at the end of this 35

Section, list hits from such PLZIP motifs. The viral sequences list d in Table VI through X potentially exhibit antiviral activity, may be useful in th the identification of antiviral compounds, and are intended to be within the scope of the invention.

5 The Examples presented in Sections 17 and 18, below, demonstrate that respiratory syncytial virus and parainfluenza virus sequences identified via such a computer search exhibit antiviral and/or structural characteristics similar to those of DP-107 or DP-178.

10 The DP-107-like and DP-178-like analogous peptides may, further, contain any of the additional groups described for DP-178, above, in Section 5.1. For example, these peptides may include any of the additional amino-terminal groups which "X" of Tables I 15 through IV may represent, and may also include any of the carboxy-terminal groups which "Z" of Tables I through IV may represent.

20 Additionally, such DP-107-like and DP-178-like peptides may furthr include DP-107-like or DP-178-like peptides, such as those listed in Tables V through X, above, containing one or more amino acid substitutions, insertions, and/or deletions. Also, analogs of such DP-107-like and DP-178-like peptides are intended to be within the scope of the invention. 25 Such analogs of the invention may exhibit increased antiviral activity, and may, further, posses increased bioavailability, and/or stability, or reduced immune recognition.

30 The DP-107-like and DP-178-like amino acid substitutions, insertions and deletions, are as described for DP-178, above, in Section 5.1. Analog modifications are as described, below, in Section 5.3.

TABLE V

**Search Results Summary for 107x178x4 and
ALLMOTI5 Motifs**

107X764		ALLM0116		
LIBRARY FILE		LIBRARY FILE		
PENV AVIRE	420-409	PENV1 FR6FY	341-378	
PENV AVIN	426-474	PENV2 FRSFV	341-378	
PENV BAEV/M	398-482	PENV AVIRE	420-472	
PENV BIV08	644-603	PENV AVIN	428-478	
PENV BIV27	673-632	PENV BAEVM	380-458	
PENV BLVAF	304-377	PENV BIV08	630-810	635-606
PENV BLVAU	304-377	PENV BIV27	669-839	664-724
PENV BLVAV	304-377	PENV BLVAF	304-378	
PENV BLVZ2	311-377	PENV BLVAU	304-379	
PENV BLVZ5	304-377	PENV BLVAV	304-379	
PENV BLVZJ	304-377	PENV BLVZ2	304-378	
PENV CAEVA	166-192	PENV BLVZ5	304-379	
PENV EIAV1	668-712	PENV BLVJ	304-379	
PENV EIAV2	668-686	PENV CAEV/C	167-186	615-720
PENV EIAV3	668-712	PENV CAEV/G	164-183	613-718
PENV ELAV5	668-686	PENV EIAV1	430-525	658-693
PENV ELAV6	668-712	PENV EIAV2	430-626	659-693
PENV ELAV7C	668-712	PENV EIAV3	430-525	659-693
PENV ELAVW	668-712	PENV EIAV5	437-526	660-694
PENV ELAVY	668-712	PENV EIAV8	430-525	659-693
PENV FIV1	617-544	PENV EIAVC	426-525	659-693
PENV FIVPE	660-680	PENV EIAVW	430-626	659-683
PENV FIVSD	639-686	PENV EIAVY	430-626	659-693
PENV FIVT2	640-679	PENV FENV1	503-565	567-604
PENV FLVC8	569-839	PENV FIVPE	610-690	718-756
PENV FLVAL	440-519	PENV FIVBD	601-688	713-764
PENV FLVLB	610-539	PENV FIVT2	609-698	714-756
PENV FLVBA	487-516	PENV FLVC9	497-549	561-596
PENV FOAMV	318-365	PENV FLVGL	478-530	542-576
PENV FSV0A	610-539	PENV FLVLB	498-560	562-596
PENV FSV0B	440-519	PENV FLVBA	475-527	539-573
PENV FSVBM	483-522	PENV FOAMV	321-356	563-693
PENV GALV		PENV FRSFB	318-354	
PENV HTL1A	342-376	PENV F8VGA	489-550	562-596
PENV HTL1C	342-376	PENV F8VGB	478-530	542-576
PENV HTL1M	342-376	PENV F8VSM	481-524	545-579
PENV HTLV2	398-370	PENV FSVBT	488-532	
PENV HYA2	644-692	PENV GALV	623-575	657-621
PENV HV181	645-694	PENV HTL1A	321-383	
PENV HV188	640-689	PENV HTL1C	316-383	
PENV HV1BN	662-690	PENV HTL1M	321-383	
PENV HV1BR	660-689	PENV HTLV2	317-377	
PENV HV1C4	617-908	PENV HY1A2	497-593	612-711
PENV HV1EL	643-691	PENV HY1B1	505-594	610-712
PENV HV1H2	645-694	PENV HY1B8	600-689	605-707
				762-838

PENV HV1H3	846-684	831-883	781-818		PENV HV1BN	801-680	808-708	783-831
PENV HV1J3	556-605	842-884	802-829		PENV HV1BR	610-680	616-717	772-841
PENV HV1JR		622-875	783-811		PENV HV1C4	610-609	628-724	770-885
PENV HV1KB	666-680	831-877	776-824		PENV HV1EL	502-581	607-709	768-829
PENV HV1MA	847-685	833-707	784-826		PENV HV1H2	606-584	616-712	767-839
PENV HV1MF	643-692	828-381	789-816		PENV HV1H3	505-594	610-712	767-843
PENV HV1MN	887-695	832-884	781-818		PENV HV1J3	617-605	622-723	770-843
PENV HV1ND	636-683	821-873	783-913		PENV HV1JR	497-588	603-704	758-835
PENV HV1OY	844-883	830-704	789-820		PENV HV1K8	611-545	656-598	618-718
PENV HV1PV	645-684	831-883	781-818		PENV HV1MA	607-580	617-714	770-825
PENV HV1RH	684-602	840-892	800-832		PENV HV1MF	603-692	622-710	768-841
PENV HV1S1	630-685	822-874	782-808		PENV HV1MN	606-595	617-713	774-841
PENV HV1S3	841-689	827-870	787-915		PENV HV1ND	498-584	601-702	767-826
PENV HV1BC	646-693	831-883	781-818		PENV HV1OY	487-583	610-711	772-849
PENV HV1W1	545-693	831-883	781-818		PENV HV1PV	605-594	610-712	767-843
PENV HV1W2	636-684	822-874	782-808		PENV HV1RH	607-603	618-721	770-852
PENV HV1Z2	642-591	828-890	780-920		PENV HV1S1	496-586	602-703	758-830
PENV HV1Z3	645-593	830-682	782-822		PENV HV1S3	494-590	607-708	763-837
PENV HV1Z6	673-601	634-878	787-928		PENV HV1BC	489-584	611-712	767-834
PENV HV1Z7H	645-694	627-868	781-923		PENV HV1W1	488-594	611-712	767-836
PENV HV2E	632-891	621-848	683-887		PENV HV1W2	489-594	602-703	768-827
PENV HV2CA	634-683	623-850	656-859		PENV HV1Z2	602-691	607-709	764-831
PENV HV2D1	623-690	606-682	644-688		PENV HV1Z6	604-693	606-711	768-840
PENV HV2A1	524-581	585-583	613-840	845-893	PENV HV1Z8	612-601	617-676	802-719
PENV HV2N2	624-681	656-583	613-840	802-889	PENV HV1ZH	622-584	612-712	777-839
PENV HV2R0	633-692	622-888			PENV HY2BE	610-595	617-680	
PENV HV2B2	622-684	589-589	648-882		PENV HV2RO	612-597	619-709	
PENV HV2B8	667-684	614-873			PENV HV2CA	601-680	608-698	
PENV HV2ST	527-664	658-588	648-892		PENV HV2G1	602-587	609-699	
PENV MCF	473-612				PENV HV2N2	488-587	609-699	
PENV MLVFP	489-615				PENV JBRV	387-422	486-827	
PENV MLVAV	517-644				PENV HV2Z2	403-455	671-805	
PENV MLVCI	810-639				PENV MCFF	473-585	637-571	
PENV MLVFI	40-81				PENV HV2B8	626-686	614-700	
PENV MLVMO	802-643				PENV MCF3	474-526	638-572	
PENV MLVRD	497-539				PENV MLVAV	603-580	612-702	
PENV MLVRX	497-638				PENV IPMAE			
PENV MLVHO	489-486	588-588			PENV MLVCA			
PENV MLVKI	459-485	582-589			PENV JBRV			
PENV MLVMO	422-470				PENV MLVFS			
PENV MLVTF	67-94				PENV MLVFF			
PENV OMVTS	42-69	180-223	780-807		PENV MLVPP	620-584	638-610	
PENV RMCFV	497-517				PENV MLVHO	604-661	683-697	
					PENV MLVKI	499-580	582-687	
					PENV MLVMO	602-654	686-690	
					PENV MLVMO	497-549	681-685	
					PENV MLVAD			

PENV SFV1	14-41	868-801		PENV MLVRK	497-549	601-598
PENV BFV3L	18-46	318-357	673-700	PENV MMTVB	477-539	668-612
PENV SIVAT	661-688	592-619	652-679	PENV MMTCG	477-639	668-612
PENV SIVAG	660-693	597-624	658-685	PENV MPMV	405-474	
PENV SIVAI	648-603	634-708	703-730	PENV MSVFB	43-98	107-141
PENV SIVAJ	690-617	651-678		PENV OMVVS	22-94	186-223
PENV SIVAT	628-684	627-864		PENV RMCFV	484-528	540-574
PENV SIVGB	689-650	784-916		PENV RSPFV	342-376	
PENV SIVH1	660-609	671-715		PENV SFV1	1-41	101-140
PENV SIVM2	168-215	277-289		PENV SFV3L	5-48	158-209
PENV SIVMK	663-609			PENV SIVA1	269-310	681-623
PENV SIVML	649-608			PENV SIVAG	666-628	651-689
PENV SIVSA	653-612	642-869	691-718	PENV SIVAI	267-291	530-370
PENV SIVSP	684-695	646-722		PENV SIVAT	264-288	549-621
PENV SIVRH	404-462			PENV SIVC2	283-291	330-365
PENV SIVV1	409-471			PENV SIVGB	686-654	677-726
PENV VILV	773-800			PENV SIVM1	114-181	468-508
PENV VILV1	780-807			PENV SIVM2	71-116	134-219
PENV VILV2	782-809			PENV SIVMK	484-505	644-692
PHEMA CYBLY	208-242			PENV SIVML	484-505	612-684
PHEMA CYBM	208-242			PENV SIVS4	486-509	617-816
PHEMA CYBL	208-242			PENV SIVBP	470-513	621-620
PHEMA CYHC	208-242			PENV SMRVA	400-466	
PHEMA CYOC	387-453			PENV ERV1	408-476	630-612
PHEMA IACIC	371-437			PENV VLV	21-92	164-222
PHEMA IABAN	381-461			PENV VILV1	21-92	184-222
PHEMA IABUD	381-451			PENV VILV2	21-92	184-222
PHEMA JACKA	382-441	494-528		PHEMA CYBLY	208-242	
PHEMA JACKO	388-426			PHEMA CYBM	208-242	
PHEMA JACKQ	388-426			PHEMA CYBQ	208-242	
PHEMA JACKV	384-443			PHEMA CYHOC	208-242	
PHEMA JADA1	381-451			PHEMA JAAIC	380-456	
PHEMA JADA2	423-463	498-843		PHEMA IABAN	384-440	
PHEMA JADA3	387-453			PHEMA IABUD	378-454	
PHEMA JADA4	418-476			PHEMA JACKA	378-454	
PHEMA JADC2	381-451			PHEMA JACKQ	108-142	375-476
PHEMA JADE1	402-453	508-633		PHEMA JACKP	380-462	494-528
PHEMA JADH1	371-437			PHEMA JACKQ	380-452	497-532
PHEMA JADH2	371-437			PHEMA JACKS	377-469	604-649
PHEMA JADH3	371-437			PHEMA JACKV	112-144	377-469
PHEMA JADH4	371-437			PHEMA JADA1	377-454	
PHEMA JADH6	371-437			PHEMA JADA2	377-476	495-547
PHEMA JADH7	371-437			PHEMA JADA3	380-453	
PHEMA JADIR	418-446			PHEMA JADA4	378-478	606-648
PHEMA JADM2	381-463			PHEMA JADC2	378-454	
PHEMA JADMZ	381-461			PHEMA JADE1	21-65	377-472
				PHEMA JADH1	384-440	

PHEMA IADU3	387-463	PHEMA IADH2	384-440
PHEMA IAEI7	387-463	PHEMA IADH3	384-440
PHEMA IAEP4	384-442	PHEMA IADH4	384-440
PHEMA IAGRE	381-461	PHEMA IADH5	384-440
PHEMA IAGU2	605-632	PHEMA IADH6	384-440
PHEMA IAGUA	504-631	PHEMA IADH7	384-440
PHEMA IAHAL	388-452	PHEMA IADIR	378-471
PHEMA IAHC3	388-457	PHEMA IADM1	21-55
PHEMA IAHC7	388-457	PHEMA IADM2	380-466
PHEMA IAHD0	388-457	PHEMA IADNY	21-55
PHEMA IAHD8	388-457	PHEMA IADNZ	378-484
PHEMA IAHQ0	388-452	PHEMA IADU1	21-55
PHEMA IAHQ4	388-452	PHEMA IADU3	380-456
PHEMA IAHK7	388-462	PHEMA IADN7	380-456
PHEMA IAHL0	388-457	PHEMA IAFFR	377-477
PHEMA IAHL0	388-467	PHEMA JAGRE	378-454
PHEMA IAHH1	388-462	PHEMA IAGU2	378-473
PHEMA IAHHM	388-462	PHEMA IAGUA	377-478
PHEMA IAHHN	388-462	PHEMA JAHAL	379-455
PHEMA IAHHN	388-457	PHEMA IAHC8	112-148
PHEMA IAHP4	388-467	PHEMA IAC7	112-148
PHEMA IAHR0	388-452	PHEMA IAHD0	380-484
PHEMA IAHB4	388-452	PHEMA IAHD8	603-537
PHEMA IAHP8	388-467	PHEMA IAHO	378-456
PHEMA IAHSW	388-457	PHEMA IAHK8	378-456
PHEMA IAHTE	388-452	PHEMA JAHK7	378-456
PHEMA IAHTO	388-466	PHEMA IAHL8	112-148
PHEMA IAHU8	388-462	PHEMA IAHL0	112-148
PHEMA IAKE	425-478	PHEMA JAHMI	378-456
PHEMA IALEN	426-476	PHEMA IAHNIM	378-456
PHEMA IAMAA	380-450	PHEMA IAHNIN	112-148
PHEMA IAMAB	385-455	PHEMA JAHPR	112-148
PHEMA IAMAO	387-453	PHEMA IAHO	378-455
PHEMA IAME1	387-453	PHEMA IAHOA	378-456
PHEMA IAME2	387-453	PHEMA IAHP	112-148
PHEMA IAME6	371-497	PHEMA IAHPB	380-484
PHEMA IAMIN	382-441	PHEMA IAHSW	112-148
PHEMA IANT6	387-453	PHEMA IAHTE	378-488
PHEMA IAPL	808-534	PHEMA JAHTO	378-456
PHEMA IAPUE	428-478	PHEMA IAHUR	378-456
PHEMA IARUD	381-451	PHEMA IAJAP	378-487
PHEMA IASE2	381-461	PHEMA JAKIE	378-478
PHEMA IABH2	608-547	PHEMA IALEN	378-478
PHEMA IASTA	384-443	PHEMA IAMAA	377-453
PHEMA IATKI	416-445	PHEMA IAMAB	382-458
PHEMA IATKM	381-461	PHEMA IAMAO	380-456
PHEMA IATKO	607-534	PHEMA IAME1	380-456
PHEMA IATKP	424-454	PHEMA IAME2	380-456
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PHEMA IATKR	381-422		PHEMA JAMEG	384-440
PHEMA IATKV	419-449	500-538	PHEMA IAMIN	108-142
PHEMA IAUDO	387-463		PHEMA IANTG	380-466
PHEMA IAUSS	426-478		PHEMA IAPIL	378-477
PHEMA IAVIT	388-484		PHEMA IAPUE	376-478
PHEMA IAWIL	424-477		PHEMA IARUD	378-464
PHEMA IAZCO	387-453		PHEMA IA8E2	378-454
PHEMA IAZH2	371-437		PHEMA IA8H2	379-474
PHEMA IAZH3	371-437		PHEMA IA8TA	112-148
PHEMA IAZIN	418-478	508-567	PHEMA IA8TK	379-471
PHEMA IAZINJ	418-478	508-547	PHEMA IATKM	378-484
PHEMA IAZUK	387-453		PHEMA IA8KO	382-470
PHEMA INBEE	400-431	438-453	PHEMA IA8LP	403-540
PHEMA INBBO	380-421	428-473	PHEMA IA8PR	378-464
PHEMA INBEN	398-428	437-481	PHEMA IA8TKW	373-472
PHEMA INBK	391-418	428-473	PHEMA IA8TA	21-55
PHEMA INBLE	389-430	438-482	PHEMA IA8UD	387-456
PHEMA INBMID	389-420	428-472	PHEMA IA8BS	376-478
PHEMA INBME	393-424	432-476	PHEMA IA8V7	381-457
PHEMA INBOR	388-428	437-481	PHEMA IA8W1	375-477
PHEMA INBSI	398-428	437-481	PHEMA IAZC0	380-466
PHEMA INBU5	391-422	430-474	PHEMA IAZH2	384-440
PHEMA INBV1	383-424	432-476	PHEMA IAZH3	384-440
PHEMA INBVK	400-431	438-483	PHEMA IAZN	379-478
PHEMA INCCA	489-571		PHEMA IAZLJ	378-478
PHEMA INCEN	483-559		PHEMA JAZUK	390-456
PHEMA INCOL	483-559		PHEMA INBBE	388-473
PHEMA INCHY	482-558		PHEMA INBBO	378-483
PHEMA INCJH	488-572		PHEMA INBEN	386-471
PHEMA INCKY	482-558		PHEMA INBK	381-463
PHEMA INCHI	482-558		PHEMA INBLE	387-472
PHEMA INCONA	482-558		PHEMA INBMD	377-482
PHEMA INCP1	483-559		PHEMA INBME	381-468
PHEMA INCP2	483-559		PHEMA INBOR	388-471
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PHEMA INCTA	483-559		PHEMA INBUS	379-464
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PHEMA NDVA	64-91		PHEMA INBVK	388-473
PHEMA NDVB	64-91		PHEMA INCCA	482-571
PHEMA NDVO	64-91		PHEMA INCEN	471-559
PHEMA NDVH	64-91		PHEMA INCJL	471-559
PHEMA NDVI	64-91		PHEMA INCHY	470-558
PHEMA NDVM	64-91		PHEMA INCJH	484-572
PHEMA NDVQ	64-91		PHEMA INCKY	470-558
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PHEMA PISH4	27-61			PHEMA INCTA	471-669	
PHEMA PISHA	27-61			PHEMA INCYA	471-559	
PHEMA PISH7	27-78			PHEMA MEASE	46-80	
PHEMA PISHU	23-70			PHEMA MEASH	46-80	
PHEMA PISHV	27-61			PHEMA MEASI	46-87	
PHEMA PISHW	27-61			PHEMA MEABY	46-87	
PHEMA PISHX	27-61			PHEMA MUMPM	34-89	
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PHEMA SENDF	78-108			PHEMA NDVA	8-62	477-529
PHEMA SENDH	78-108			PHEMA NDVB	1-49	
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PHEMA SV41	22-82	384-521		PHEMA NDVQ	1-49	
PHEMA VACCC	119-148	176-202	216-243	PHEMA NDVTG	1-49	
PHEMA VACCI	109-148	176-202	216-243	PHEMA NDVU	1-49	
PHEMA VACCT	118-148	176-202	216-243	PHEMA NDVY	1-49	
PHEMA VACCV	109-148	176-202	216-242	PHEMA PHODV	39-73	
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PVF08 VACCV	33-60			PHEMA PISHU	13-110	394-428
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PVF12 VACCC	10-37	113-140	654-581	PHEMA PISHX	13-110	394-428
PVF12 VACCP	10-37	113-140	654-581	PHEMA PI4HA	64-88	
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PVG01 VARV	226-262	301-335		PHEMA SV41	18-62	397-421
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PVG03 HVEB	146-176			PVENV BEV	166-229	
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PVG07 DHVII	71-98			PVENV THOGV	213-354	

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PVGL2_IBVB	809-835	875-802	1056-1080	PVG37_HSV1	17-80	
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PVGL2_IBVM	808-836	875-902	1056-1080	PVG39_HSV1	124-168	286-300
PVGLB_EBV	95-122	631-858		PVG39_SPV1R	8-49	162-198
PVGLB_HCMVA	26-88	397-124	440-467	PVG39_SPV4	6-54	67-121
PVGLB_HCMVT	50-88	397-124	435-482	PVG43_HSV1	116-160	282-296
PVGLB_HSVB1	427-464		852-878	PVG45_HSVBA	121-162	
PVGLB_HSVB2	447-474			PVG49_HSV1	45-88	939-1078
PVGLB_HSVBC	426-463			PVG48_HSV1	168-207	
PVGLB_HSVE1	443-470	634-861		PVG48_HSVBA	360-417	611-888
PVGLB_HSVE4	486-513	616-843		PVG49_HSV5A	68-102	
PVGLB_HSVEA	443-470	634-861		PVG48_AMEPV	4-38	
PVGLB_HSVEB	443-470	634-861		PVG44_SPV4	88-130	
PVGLB_HSVEL	443-470	933-980		PVG51_HSV1	34-73	88-123
PVGLB_HSVID	93-120	382-378		PVG51_HSVBA	28-70	123-157
PVGLB_MCMV6	381-408	441-475		PVG53_Hsv1	67-127	162-186
PVGLC_HSV11	488-510			PVG54_HSV1	385-396	
PVGLC_HSV1K	489-510			PVG55_HSV1	101-135	
PVGLC_HSVEB	124-151			PVG56_HSVBA	126-178	
PVGLC_HSVNB	63-97			PVG58_HSV1	161-182	678-612
PVGLC_HSVNG	62-98			PVG59_HSV1	110-122	881-123
PVGLC_HSVNM	63-97			PVG59_HSVBA	168-209	
PVGLC_VZMD	286-322			PVG65_SPV1R	85-103	
PVGLC_VZV8	286-322			PVG61_HSV1	265-289	
PVGLC_HSV2	111-148			PVG63_HSV1	546-584	
PVGLF_HSV1	38-86	154-202	216-243	PVG65_HSV1	808-839	1213-1264
PVGLF_BRSA	38-86	154-202	216-243	PVG66_HSV1	184-188	328-410
PVGLF_BRSC	38-86	154-202	216-243	PVG67_HSV1	319-413	601-646
PVGLF_BRSVR	38-86	154-202	216-243	PVG68_HSV1	245-288	
PVGLF_CDVO	262-263	340-387		PVG72_HSV1	447-484	723-757
PVGLF_HRSV1	38-86	154-203	442-471	PVG75_HSV1	271-305	388-422
PVGLF_HRSV4	38-86	154-202	213-243	PVG88_SPV1R	6-51	
PVGLF_HRSV5	38-86	154-202	216-243	PVG89_SPV1R	142-179	1233-1267
PVGLF_HRSVR	38-86	154-202	213-243	PVG93_HCMVA	10-44	
PVGLF_ME8E	228-262			PVG12_CVBF	842-876	850-886
PVGLF_ME8I	231-268			PVG12_CVBL9	860-885	873-1109
					1263-1305	

PVGLF MEASY	228-282		PVG12_CVBLY	642-876	650-885	883-1108	1283-1305
PVGLF MUMPM	20-54	447-486	PVG12_CVBM	642-876	850-885	983-1108	1283-1305
PVGLF MUMPR	20-54	447-486	PVG12_CV/BQ	642-876	850-885	983-1108	1283-1305
PVGLF MUMPS	161-178	428-511	PVG12_CV/BV	642-876	850-885	983-1108	1283-1305
PVGLF NDVA	161-178	428-512	PVG12_CVH22	770-818	1066-1112		
PVGLF NDVB	161-178	428-512	PVG12_CVM4	843-884	1001-1117	1270-1315	
PVGLF NDVI	161-178	428-512	PVG12_CVMA5	591-632	949-1079	1216-1263	
PVGLF NDVA	161-178	428-512	PVG12_CV/MJH	602-643	860-878	1128-1174	
PVGLF NDVT	161-178	428-512	PVG12_CV/P8	69-110	446-482	692-739	889-923
PVGLF NDVA	161-178	428-512	PVG12_CV/PU	69-110	446-480	680-731	887-921
PVGLF NDVU	161-178	428-512	PVG12_CV/R8	224-258	488-509	885-888	818-882
PVGLF PHOBV	38-63	221-282	PVG12_CV/PRM	224-258	488-509	885-888	818-882
PVGLF P11KC	147-174	210-288	PVG12_EBV	68-102			
PVGLF P12KH	90-117	141-175	PVG12_FIPV	188-245	451-485	695-738	882-826
PVGLF P12HG	80-117	141-176	PVG12_IBV6	791-905			
PVGLF P12HT	80-117	141-176	PVG12_IBV3	437-448	772-904	1056-1080	
PVGLF P13B	115-182	207-241	PVG12_IBD2	773-905	1067-1091		
PVGLF P13H	115-182	207-241	PVG12_IBK	437-478	772-904	1056-1080	
PVGLF RINDX	224-286	489-505	PVG12_IBVM	437-478	772-904	1056-1080	
PVGLF RINDL	224-286	489-506	PVG1B_HCMVA	43-88	128-162	438-484	844-878
PVGLF SENDB	122-149	211-248	PVG1B_HCMVT	22-68	128-162	437-485	845-879
PVGLF SENDF	122-149	211-245	PVG1B_HS/1	828-890			
PVGLF SENUDH	122-149	211-245	PVG1B_HS/VIF	827-889			
PVGLF SENDJ	122-149	211-245	PVG1B_HS/VIK	827-889			
PVGLF SENDZ	122-149	211-245	PVG1B_HS/VIP	828-890			
PVGLF SV41	144-186	241-269	PVG1B_HS/V23	828-890			
PVGLF SV6	137-171	417-444	PVG1B_HS/V2H	826-890			
PVGLF THTV	124-161	193-200	PVG1B_HS/V28	817-871			
PVGLG BEFY	823-667		PVG1B_HS/6U	37-71	166-223		
PVGLG BRBVC	92-123		PVG1B_HS/V1	858-913			
PVGLG HR8V1	63-93		PVG1B_HS/V2	440-474	848-902		
PVGLG HR8V4	69-107		PVG1B_HS/VBC	863-900			
PVGLG HR8VS	243-273		PVG1B_HS/V1	642-578	911-981		
PVGLG HR8V8	68-93		PVG1B_HS/EA	474-516	847-900		
PVGLG HR8V4	271-289		PVG1B_HS/EA	642-570	911-981		
PVGLG HBVEB	383-410		PVG1B_HS/EB	643-578	911-981		
PVGLG RABVT	498-518		PVG1B_HS/EL	542-578	910-980		
PVGLG YSV10	472-499		PVG1B_HS/MD	380-435	648-683	787-845	
PVGLH EBV	540-679	618-848	PVG1B_HS/8A	240-288	406-447		
PVGLH HCMVA	107-138	270-297	PVG1B_MCMV8	208-280	427-475	693-778	880-884
PVGLH HCMVT	109-138		PVG1B_PRVIF	847-881			
PVGLH HS/80	62-89	386-403	PVG1B_VZVD	92-133	688-630	805-887	
PVGLH HS/8A	388-416		PVG1C_HS/1	489-510			
PVGLI HCMVA	47-111		PVG1C_HS/1K	468-510			
PVGLM BUNGE	612-649	614-841	PVG1C_HS/2	442-476			
PVGLM BUNL7	813-860		PVG1C_HS/23	443-477			
PVGLM BUNYY	340-374	804-935	PVG1C_HS/BC	238-269			

PVGLM DUGBV	646-972		PVGIC HSVEB	182-218
PVGLM HANTH	73-100	683-720	PVALC HSVMB	63-87
PVGLM HANTH	76-102		PVALC HSVMG	62-98
PVGLM HANTL	76-102		PVALC HSVMM	63-97
PVGLM HANTY	76-102		PVGIC PRVIF	183-236
PVGLM PHV	68-88		PVALC PZAV	280-321
PVGLM PUUH	72-110		PVGIC VZVB	280-321
PVGLM PUUHS	72-110		PVALD HEVEA	88-123
PVGLM SECUR	73-100	613-540	PVALD HSVEB	139-173
PVGLM SEOUS	73-100	613-540	PVALD HSVEK	138-173
PVGLN BEPV	523-584		PVGLE HSVI1	111-146
PVGLP BEV	48-82	1146-1179	PVALE HSVI2	111-158
PVGLX HSVEB	17-44	413-444	PVGLF BRSVA	148-202
PVGLX PRVRI	427-461		PVGLF BRBVC	148-202
PVGLY JUNIN	14-41		PVGLF BRSVR	148-202
PVGLY LAS60	86-113		PVGLF CDVO	228-297
PVGLY MOPEI	86-113	316-346	PVGLF HRSV1	116-203
PVGLY PIARV	334-375		PVGLF HRSVA	116-202
PVGLY TACV	108-138	316-350	PVGLF JPSVL	116-202
PVGLY TACV6	303-339		PVGLF HRBSR	116-202
PVGLY TACV7	302-337		PVGLF MEASE	116-184
PVGLY TACV7	303-338		PVGLF MEASI	119-187
PVGL2 HSVEK	17-44		PVGLF MEASY	116-184
PVGNM BPNV	403-430		PVGLF MUMPM	20-54
PVGNM CPSMV	182-221		PVGLF MUHPR	20-54
PVGPB EBV	104-148		PVGLF MUMPS	20-54
PVMA REOVL	280-317		PVGLF NDVA	117-182
PVM21 REOVD	626-682		PVGLF NDVIB	122-182
PVM22 REOVD	624-681		PVGLF NDVI	133-182
PVM2 REOJ	624-681		PVGLF NDVIM	117-179
PVM3 REOVD	168-180	343-370	PVGLF NDVT	117-182
PVM42 BRBVA	124-162		PVGLF NDVTA	122-182
PVM42 HSVEA	124-161		PVGLF NDVU	122-182
PVMAT BRBVA	219-240		PVGLF PHODV	28-83
PVMAT HSVA	216-249		PVGLF PI1HC	129-174
PVMAT INCU	161-186	631-680	PVGLF PI2H	93-183
PVMAT SV41	323-363		PVGLF PI2HQ	93-183
PVMAT NDVA	247-274		PVGLF RINDL	122-180
PVME1 PI2HTT	98-123		PVGLF PI2HT	93-185
PVMAT BRBVA	201-231		PVGLF PI3B	117-182
PVMAT PI3H	201-231		PVGLF PI3H	117-182
PVMAT PI3H4			PVGLF PI3H4	117-182
PVMAT INCU	161-186		PVGLF RNDK	112-180
PVME1 CYB41	175-209		PVGLF RNDL	112-180
PVME1 CYTKE	176-209		PVGLF SENDS	127-188
PVME1 IBVB	21-48	184-218	PVGLF SENDB	127-188
PVME1 IBVB	21-48	184-219	PVGLF SENDF	127-188
PVME1 IBVB2	21-48	184-218	PVGLF SENDH	127-188
PVME1 IBVK		184-216	PVGLF SENDJ	127-188
			PVGLF SENDZ	127-188

PVMP CAMYC	220-264	273-324	PVGLF 8V41	88-188	484-508
PVMP CAMYD	28-68	220-264	273-324	103-171	241-276
PVMP CAMYE	227-284	273-324	PVGLF 8V5	105-161	180-224
PVMP CAMYN	220-264	273-324	PVGLF TRIV	508-612	457-498
PVMP CAMYS	220-264	273-324	PVGLG BRSVC	30-70	104-138
PVMP CAMYV	220-264	273-324	PVGLG HRSV1	30-81	
PVMP CERV	28-53	100-127	PVGLG HRSV2	30-85	
PVMP BOCHY	4-31	78-118	PVGLG HRSV3	30-86	
PVMTA HBHBE	284-328		PVGLG HR8V4	30-107	
PVMT1 DRWII	38-65	237-284	PVGLG HRSV5	30-85	
PVMTB MYXVL	163-190		PVGLG HRSV8	30-86	
PVMTB MY2XVL	465-492		PVGLG HRSV7	30-85	
			PVGLG HRSV8	30-81	
			PVGLG HR8VA	30-87	
			PVGLG HRSVL	25-86	
			PVGLG HSVE4	271-306	
			PVGLG SIGMA	344-381	484-488
			PVGLG BYNV	488-523	
			PVGLG VH9VO	383-397	
			PVGLG VS9IG	476-510	
			PVGLH EBV	63-97	180-201
			PVGLH HCMVA	103-137	210-311
			PVGLH HCMVT	102-136	682-740
			PVGLH HBV11	447-481	
			PVGLH H9V1E	447-481	
			PVGLH HSV8G	387-406	
			PVGLH HVBC	384-416	
			PVGLH HSVE4	334-378	414-456
			PVGLH HVEB	327-372	407-448
			PVGLH HSVSA	32-86	374-453
			PVGLH MCMLV	440-474	
			PVGLH PRVKA	226-260	
			PVGLH PRVN3	226-260	
			PVGLH PRVRI	226-260	
			PVGLH YZVD	485-506	
			PVBLI HCKVVA	47-111	323-359
			PVGLM BUNGE	612-687	685-737
			PVGLM BUNL7	643-677	916-950
			PVGLM BUNSH	843-877	
			PVGLM BUNYY	340-374	804-863
			PVGLM DUBBY	837-989	1239-1300
			PVGLM HANTB	683-727	
			PVGLM HANTH	72-108	
			PVGLM HANTL	72-108	
			PVGLM HANTV	72-108	
			PVGLM PHV	73-111	
			PVGLM PTPV	149-261	

PVALM SEOUR	694-729
PVALM SEOUS	683-730
PVALN BEPV	377-414
PVALP BEV	43-82
PVALX HSVEB	177-282
PVALX PRVRI	420-481
PVALY JUNIN	301-349
PVALY LASBG	317-380
PVALY LASJ	316-381
PVALY LYCYA	333-387
PVALY LYCVW	124-168
PVALY MOPEI	316-369
PVALY PIARY	324-375
PVALY TACY	316-383
PVALY TACV6	303-351
PVALY TACY7	302-350
PVALY TACYT	303-361
PVANB CPMV	835-889
PVANH BRAN	143-177
PVANM CPMV	160-201
PVANM CP8MV	192-226
PVANM RCMV	837-871
PVAPB EBV	94-149
PVM01 VACCC	5-59
PVM1 REOVL	287-321
PVM21 REOVD	416-450
PVM22 REOVD	416-450
PVM2 REOVJ	416-450
PVM2 REOVL	416-450
PVM3 REOVD	135-180
PVM42 BR8VA	42-90
PVM42 HR8VA	42-80
PVMAT CDVO	193-234
PVMAT INCJ	73-14
PVMAT NDVA	310-359
PVMAT NDVB	324-358
PVMAT P13B	88-133
PVMAT P13H4	89-133
PVMAT RABVA	69-103
PVMAT RABVC	69-103
PVMAT RABVE	69-103
PVMAT RABVN	69-103
PVMAT RABVP	69-103
PVMAT RABVB	69-103
PVMAT SYNV	246-280
PVMAT VS8IG	198-232
PVME1 CVBM	175-209

PVME1_CVFFS	98-148	212-267
PVME1_CVPPU	212-267	
PVME1_CVPRM	212-267	
PVME1_CVTK8	2B-62	176-208
PVME1_FIPY	212-267	
PVME1_IBV6	21-66	177-218
PVME1_IBVB	21-66	177-218
PVME1_IBVB2	21-66	177-218
PVME1_IBVK	36-64	
PVMP_CAMVC	187-264	270-324
PVMP_CAMVD	187-264	270-324
PVMP_CAMVE	187-264	270-324
PVMP_CAMVN	187-264	270-324
PVMP_CAMVB	187-264	270-324
PVMP_CAMVW	187-264	270-324
PVMP_CERV	212-268	
PVMP_FAVD	217-261	
PVMP_BOCMV	76-118	
PVMSA_HPB08	272-313	324-381
PVMSA_HPBDC	271-312	323-380
PVMSA_HPBDC	234-276	286-323
PVMSA_HPBDW	272-313	324-381
PVMSA_HPB09	210-244	
PVMSA_HPBHE	284-328	
PVMSA_WAV1	208-242	
PVMSA_WAV59	213-247	
PVMSA_WAV7	213-247	
PVMSA_WAV81	213-247	
PVNT1_DHVII	201-236	
PVNT1_IANN	82-126	174-222
PVNT1_IABAN	82-126	174-222
PVNT1_IACAO	31-79	
PVNT1_IAFOW	92-126	174-222
PVNT1_IAPFR	92-126	174-222
PVNT1_IAPFW	92-126	174-222
PVNT1_IALE1	92-126	174-222
PVNT1_IALE2	92-126	174-222
PVNT1_IAMAN	92-126	174-222
PVNT1_IAPOC	92-126	174-222
PVNT1_IAPUE	92-126	174-222
PVNT1_IAUDIO	92-126	174-222
PVNT1_IAWIL	92-126	174-222
PVNT1_IAZI1	92-126	174-222
PVNT1_INBAC	176-208	
PVNT1_INBAD	176-208	
PVNT1_INBLE	176-208	
PVNT1_INBSI	176-209	

PVMT2 INBAC	132-184
PVMT2 INBAD	132-184
PVMT2 INBLE	132-184
PVMT2 INBBI	132-184
PVMT2 INBBL	132-184
PVMT8 MY7AVL	46-80 145-187

TABLE VI

Search Results Summary for PCTLZIP,
P1CTLZIP, and P2CTLZIP Motifs

PCTZIP	PICT2ZIP	LIBRARY FILE	LIBRARY FILE	LIBRARY FILE	P2CTZIP
PENV FOAMV	461-498	PENV BV08	434-460	PENV BV06	628-542
PENV HVIMA	438-453	PENV BV27	463-478	PENV BV27	664-671
PENV HVIMP	169-188	PENV FOAMV	481-488	PENV FENVI	30-47
PENV HVRH	445-460	PENV HV1KB	782-788	PENV FIVPE	781-798
PENV HV1C	188-201	PENV HV1MA	437-453	PENV FIVSD	778-799
PENV HV1Z	128-138	PENV HV1MF	183-198	PENV FIVT2	780-797
PENV HV1ZH	438-453	PENV HV1RH	444-460	PENV FLVC8	38-55
PENV HV2BE	760-765	PENV HV161	738-754	PENV FLVGL	606-622
PENV HV2C1	741-768	PENV HV18C	188-201	PENV FLVLB	625-642
PENV HV2G1	74-768	PENV HV122	123-138	PENV FLVBA	602-610
PENV HV2Z	742-767	PENV HV123	117-133	PENV FOAMY	710-727
PENV HV2Z0	751-788	PENV HV1ZH	437-463	PENV FSYGA	625-642
PENV HV2BB	743-768	PENV HV2BE	750-766	PENV FBVGB	605-622
PENV HV2BT	746-760	PENV HV2D1	741-756	PENV FBVBM	608-626
PENV J8RV	104-119	PENV HV2G1	741-756	PENV HV1QY	123-140
PENV MMIVB	618-633	PENV HV2NZ	742-757	PENV HV122	410-427
PENV MMIVG	618-633	PENV HV2R0	751-766	PENV HV123	154-171
PENV SIVMK	138-164	PENV HV2SB	743-768	PENV HV2CA	760-787
PENV SIVML	138-164	PENV HV2ST	746-760	PENV MCFF	600-617
PHEMA CVBLY	391-408	PENV_JBV	104-119	PENV MCFF3	601-618
PHEMA CVBM	391-408	PENV_MCF	397-413	PENV MLVAV	630-647
PHEMA CVBO	391-408	PENV_MCF3	397-413	PENV MLVCB	625-642
PHEMA CVHOC	391-408	PENV_MLYAV	427-443	PENV MLVFB	639-656
PHEMA_CVMAG	402-417	PENV_MLVCB	427-438	PENV MLVFF	639-656
PHEMA_CVMS	403-418	PENV_MLYHO	428-438	PENV MLVFP	639-656
PHEMA_INEA	288-310	PENV_MLYMO	429-442	PENV MLVHO	620-643
PHEMA_INBE	303-318	PENV_MLYRD	424-440	PENV MLVKU	167-184
PHEMA_INBO	293-308	PENV_MLYRK	424-440	PENV MLVMO	628-646
PHEMA_INBN	301-318	PENV_MMIVB	618-633	PENV MLVRD	624-641
PHEMA_INBU	288-301	PENV_MMIVQ	618-633	PENV MLVRK	624-641
PHEMA_INCL	298-311	PENV_BPV1	884-890	PENV MSVFB	170-187
PHEMA_INHK	29-308	PENV_BPV3L	881-877	PENV RMCFV	603-620
PHEMA_INIB	288-303	PENV_BIVGB	93-109	PENV_BFV1	710-727
PHEMA_INID	299-314	PENV_BIVMK	138-164	PENV_BFV3L	707-724
PHEMA_INLE	302-317	PENV_BIVML	138-164	PENV_BIVMI	768-783
PHEMA_INMD	282-307	PENV_BIVSA	804-822	PENV_BIVMK	765-782
PHEMA_INME	288-311	PENV_BIVSP	810-826	PENV_BIVML	764-781
PHEMA_INNA	288-303	PHEMA_COVO	36-52	PENV_BIV84	768-786
PHEMA_INOR	301-318	PHEMA_CVBLY	391-408	PENV_BIVSP	773-790
PHEMA_INSI	201-316	PHEMA_CVBM	391-406	PENV_SMRVH	638-653
PHEMA_INSSJ	288-313	PHEMA_CVBSQ	391-406	PENV_SMSAV	42-59
PHEMA_INUB	284-309	PHEMA_CVHOC	391-406	PHEMA_CDOV	36-53
PHEMA_INVI	298-311	PHEMA_CVMA6	402-417	PHEMA_CVBLV	391-408
PHEMA_INVK	303-318	PHEMA_CVMS	403-418	PHEMA_CVBM	391-408
PHEMA_INVB	288-301	PHEMA_IAC	237-263	PHEMA_CVHQ	391-409

PHEMA MUMPM	133-149	PHEMA JABAN	221-237	PHEMA CVHOC	391-408	
PHEMA MUMPR	133-148	PHEMA JABUD	234-250	PHEMA IAAIC	322-339	
PHEMA MUMPS	133-148	PHEMA JACKA	234-250	PHEMA IABAN	308-323	
PHEMA P11HW	245-380	PHEMA JACKG	231-247	PHEMA JACKU	320-337	
PHEMA P12H	65-80	PHEMA JACKV	230-246	PHEMA JACKA	320-337	
PHEMA P12HT	65-80	PHEMA JADA1	234-250	PHEMA JACKG	316-333	
PHEMA RINDK	368-383	PHEMA JADA3	237-253	PHEMA JACKP	302-319	
PHEMA SV5	7-84	PHEMA JADC2	234-250	PHEMA JACKQ	302-319	
PHEMA SV6CM	7-84	PHEMA JADH1	221-237	PHEMA JACKS	316-336	
PHEMA SV6CP	7-84	PHEMA JADH2	221-237	PHEMA JACKY	316-332	
PHEMA SV6LN	7-84	PHEMA JADH3	221-237	PHEMA IADAI	320-337	
PYENV DHV11	42-57	PHEMA JADH4	221-237	PHEMA IADAS	322-338	
PYFP7 CAPW	89-104	PHEMA JADH5	221-237	PHEMA IADCE	320-337	
PYFUS VACG8	72-97	PHEMA JADH6	221-237	PHEMA IADCH1	308-323	
PYG01 BPP22	242-257	PHEMA JADH7	221-237	PHEMA IADH2	308-323	
PYG01 HSVEB	189-194	PHEMA JADM2	237-263	PHEMA IADH3	308-323	
PYG01 HSV11	210-226	317-332	PHEMA JADN2	234-260	PHEMA IADH4	308-323
PYG06 BPT4	184-189	PHEMA JAEN	221-237	PHEMA JADH6	308-323	
PYG07 BPT4	88-90	PHEMA JAEN7	237-263	PHEMA IADH7	308-323	
PYG08 HSV11	134-149	PHEMA IAFFR	230-246	PHEMA IADM2	322-338	
PYG10 BPPH2	183-198	PHEMA JAHAL	238-262	PHEMA IADN2	320-337	
PYG10 BPPZA	183-198	PHEMA JAHLAR	235-261	PHEMA IADU3	322-339	
PYG10 HSVA	108-124	PHEMA JAHC8	230-246	PHEMA JAENG	308-323	
PYG16 BPP1	81-96	PHEMA JAHC7	230-246	PHEMA JAEN7	322-338	
PYG18 BPT4	488-483	PHEMA IAHCD	230-246	PHEMA JAFFR	316-332	
PYG25 BPT4	97-112	PHEMA IAHDE	230-246	PHEMA JAIGRE	320-337	
PYG29 HS/V1	20-38	PHEMA IAHFO	238-252	PHEMA JAGU2	320-337	
PYG30 BPPH8	11-94	PHEMA IAHK8	236-262	PHEMA JAIGUA	316-338	
PYG36 BPOX2	22-37	PHEMA IAHK7	236-262	PHEMA JAHAL	321-339	
PYG39 HS/VA	108-123	PHEMA IAHL	230-246	PHEMA IAHK6	316-332	
PYG37 BPT2	1263-1268	PHEMA IAHL0	230-246	PHEMA IAHC7	316-332	
PYQ37 HS/V1	284-299	PHEMA IAHHI	238-262	PHEMA IAHCD	316-332	
PYQ55 HS/V1	22-37	143-168	PHEMA IAHNM	236-262	PHEMA JAHDE	316-332
PYQ66 HS/V1	288-283	PHEMA JAHRO	238-262	PHEMA JAHO	321-338	
PYQ88 HS/V1	102-117	PHEMA IAHSA	238-262	PHEMA IAHK8	321-338	
PYQ99 HS/V1	267-282	PHEMA JAHPB	230-246	PHEMA IAHK7	321-338	
PYQ65 HS/V1	816-833	PHEMA IAHSW	230-246	PHEMA IAHE	316-332	
PYQ8 BPPH2	234-249	PHEMA IAHTE	238-262	PHEMA IAHLO	316-332	
PYQ9 BPPZA	234-249	PHEMA IAHTO	238-262	PHEMA JAHHI	321-338	
PYQ9 BPPVR	87-72	PHEMA IAHUR	238-262	PHEMA IAHNM	321-338	
PYQF BPPHX	234-249	PHEMA IAIE	238-281	PHEMA IAHHN	916-322	
PYQL2 CVBF	264-279	PHEMA IALEN	238-261	PHEMA JAHPR	316-332	
PYQL2 CVB19	264-279	PHEMA IAMAA	233-249	PHEMA JAHR	321-338	
PYQL2 CVBLY	264-279	PHEMA IAMAB	238-264	PHEMA IAHSA	321-338	
PYQL2 CVBM	264-279	PHEMA IAMAO	237-263	PHEMA IAHPSP	316-332	
PYQL2 CVBQ	264-279	PHEMA IAME1	237-253	PHEMA IAMSW	316-332	
PYQL2 CVBV	264-279	PHEMA IAME2	237-253	PHEMA IAHTE	321-339	

PVQL2_CVFF8	442-467	PHEMA JAME#	221-237	PHEMA JAHTO	321-338	
PVQL2_CVPPU	440-465	604-619	PHEMA JAMIN	86-101	PHEMA JAHUR	321-333
PVQL2_CVPRB	218-233	PHEMA JANT#	237-263	PHEMA JA-JAP	317-334	
PVQL2_CVPRM	218-233	PHEMA JAQU7	221-237	PHEMA JAMAA	319-338	
PVQL2_IBV6	1068-1071	PHEMA JARUD	234-250	PHEMA JAMAB	324-341	
PVQL2_IBVB	1065-1070	PHEMA JASE2	234-250	PHEMA JAMAO	322-339	
PVQL2_IBVD2	1065-1071	PHEMA JASH2	234-250	PHEMA JAME1	322-339	
PVQL2_IBVK	1065-1070	PHEMA JASTA	230-248	PHEMA JAME2	322-339	
PVQL2_IBVM	1065-1070	PHEMA JATAI	236-261	PHEMA JAMES	308-323	
PVQLB_HS7/8A	701-716	PHEMA JATKM	234-250	PHEMA JAMIN	318-333	
PVQLB_PRV/F	203-218	PHEMA JATKO	233-248	PHEMA JANT6	322-339	
PVQLC_HSVBC	475-480	PHEMA JATKR	230-248	PHEMA JAPIL	320-337	
PVQLC_HSVE4	444-459	PHEMA JATKW	229-246	PHEMA JAQU7	308-323	
PVQLC_HSVEB	427-442	PHEMA JAUDO	237-253	PHEMA JARUD	320-337	
PVGLC_PRV/F	446-461	PHEMA JAUSS	236-261	PHEMA JA8E2	320-337	
PVQLD_HS11	78-94	PHEMA JAVI7	238-284	PHEMA JASH2	321-338	
PVQLD_HS2	79-94	PHEMA JAXIA	238-261	PHEMA JASTA	315-332	
PVQLF_BRBYA	285-280	PHEMA JA2CO	237-253	PHEMA JATKM	320-337	
PVQLF_BR9/C	285-280	PHEMA JAZH2	221-237	PHEMA JAUDO	322-339	
PVQLF_BR9/R	285-280	PHEMA JAZH3	221-237	PHEMA JAVI7	323-340	
PVQLF_HRBV1	285-280	PHEMA JAZK	237-263	PHEMA JAZCO	322-339	
PVQLF_HRSVA	285-280	PHEMA JBA	116-131	PHEMA JAZH2	308-323	
PVQLF_HRSV1	285-280	PHEMA INBB	123-139	PHEMA JAZH3	308-323	
PVQLF_HRSV4	285-280	PHEMA INBO	116-132	PHEMA JAZUK	322-339	
PVQLF_HUMPS	6-64	PHEMA INBN	123-138	PHEMA MUMPM	101-118	
PVQLI_VZ/D	218-283	PHEMA INBU	108-124	PHEMA MUMPR	101-118	
PVQLM_HANTS	800-916	PHEMA INBL	119-135	PHEMA MUMPS	101-118	
PVQLM_PTPV	743-758	PHEMA INBK	118-132	PHEMA NOVA	83-110	
PVQLM_SEOUR	901-916	PHEMA INBIB	108-124	PHEMA NDV8	83-110	
PVQLM_SEOUS	800-916	PHEMA INBD	120-136	PHEMA NDVD	83-110	
PVQLY_LASBG	426-441	PHEMA INBLE	123-139	PHEMA NDVH	83-110	
PVQLY_LASBJ	427-442	PHEMA INBM	113-129	PHEMA NDVJ	83-110	
PVQLY_MPEI	426-440	PHEMA INBME	116-132	PHEMA NDVW	83-110	
PVM3_RECVD	621-638	PHEMA INBN	288-303	PHEMA NOVO	83-110	
PVMBA_HPB09	380-396	PHEMA INBOR	301-316	PHEMA NDVTQ	83-110	
PVMBA_WHV9	187-202	PHEMA INBBI	123-139	PHEMA NDVU	83-110	
PVMBA_WHV1	378-393	PHEMA INBSJ	119-135	PHEMA PHODV	38-53	
PVMBA_WHV69	383-398	PHEMA INBLS	286-311	PHEMA PI1HW	486-503	
PVMBA_WHV7	383-396	PHEMA INBVI	108-124	PHEMA PI3B	111-128	
PVMBA_WHV8	383-398	PHEMA INBVK	123-139	PHEMA PI3HA	111-128	
PVMBA_WHV81	383-398	PHEMA INBYB	109-124	PHEMA PI3HA	111-128	
PVMBA_WHV90	234-249	PHEMA MUMPM	133-148	PHEMA PI3HT	111-128	
PVMT2_JAANN	25-40	PHEMA MUMPR	133-148	PHEMA PI3HU	111-128	
PVMT2_JABAN	25-40	PHEMA MUMPS	133-148	PHEMA PI3IV	111-128	
PVMT2_JAFDW	25-40	PHEMA P11HW	346-360	PHEMA PI3HW	111-128	
PVMT2_JAFPR	25-40	PHEMA P12H	65-81	PHEMA PI3HX	111-128	
PVMT2_JAHPW	25-40	PHEMA P12HT	65-81	PHEMA PI4HA	80-87	

PVMT2_IALE1	26-40	PHEMA_P13B	324-340		PHEMA_BV41	65-102
PVMT2_IALE2	25-40	PHEMA_P13H4	324-340		PHEMA_BS5	84-101
PVMT2_JAMAN	25-40	PHEMA_P13HA	324-340		PHEMA_BS6CM	84-101
PVMT2_IAPUE	26-40	PHEMA_P13HT	324-340		PHEMA_BS6CP	84-101
PVMT2_IASIN	25-40	PHEMA_P13HU	324-340		PHEMA_BS6LN	84-101
PVMT2_IAUDIO	25-40	PHEMA_P13HV	324-340		PVFO5_VACCC	280-287
PVMT2_IAWIL	26-40	PHEMA_P13HW	324-340		PVFO5_VACCP	280-287
PVMT2_IMYXIL	226-241	PHEMA_P13HX	324-340		PVFO5_VACCV	281-288
		PHEMA_RINDK	368-383		PVFO9_VACCC	176-193
		PHEMA_BS6	7-94		PVFO9_VACCV	176-183
		PHEMA_BS6CM	7-94		PVFO9_HSVSA	209-228
		PHEMA_BS6CP	7-94		PVFO8_HSVII	173-190
		PHEMA_BS6LN	7-94		PVFO9_HSVII	648-665
		PVENV_DHVII	42-57		PVFO3_HSVII	109-128
		PVENV_EAV	26-41		PVFO7_HSVII	171-188
		PVFP2_FWFPV	89-104		PVFO2_HSVII	1262-1269
		PVFP7_CAPIK	89-104		PVQFL1_BYB	3079-3080
		PVFS5_VACC8	72-87		PVFL2_BYB6	1094-1111
		PVFO01_HSVEB	168-184		PVQLB_HSVF1	738-759
		PVFO01_HSVII	209-225	317-332	PVQLB_HSVF4	676-692
		PVFO08_HSVI	134-149		PVQLB_HSVEA	736-753
		PVFO10_HSVBA	108-124		PVQLB_HSVEB	736-753
		PVGL1_HSVII	103-119		PVQLB_HSVEL	736-753
		PVGL2_HSVI	270-288		PVQLB_LTV6	697-714
		PVGL1_SPV1R	76-92		PVQLB_LTV8	607-624
		PVGL9_HSVII	20-35		PVQLB_LTV7	607-624
		PVGS9_EPOX2	22-37		PVQLC_PAVIF	180-197
		PVGS80_HBVBA	108-123		PVQLF_QVID	468-498
		PVGS7_HBVII	284-288		PVQLF_BYB	401-419
		PVGS1_HBVII	244-260		PVALH_HCMVA	368-382
		PVGS46_HBVII	1244-1260		PVALH_HCMVT	384-381
		PVGS5_HBVII	22-37	143-158	PVALH_HSVI1	246-282
		PVGS6_HSVII	288-283		PVALH_HSVIE	246-282
		PVGS8_HBVII	101-117		PVALI_BS6	43-60
		PVGS9_HBVSA	130-148	330-346	PVALM_BSUNL7	61-88
		PVGS9_HSVII	267-282		PVALM_BUNSH	61-88
		PVGS8_HSVII	362-378	518-633	PVALM_PUUMH	712-728
		PVGS1_HBVSA	86-105		PVALM_PUUMS	712-728
		PVGS9_BPFH2	294-249		PVALM_RVFV	344-361
		PVGS_BPFZA	234-248		PVALY_LA89Q	12-84
		PVGS_SPV1R	67-72		PVALY_LA88J	12-84
		PVGS1_BYB	2210-2220		PVALY_LYCVIA	12-94
		PVGL2_CYBF	123-138	174-180	PVALY_LYCVW	12-84
		PVGL2_CVBL9	123-139	174-180	PVALY_MOPEI	12-94
		PVGL2_CVBLY	123-139	174-180	PVMI_BEODO	280-297
		PVGL2_CVBM	123-139	174-180	PVMI_BEODV	280-297
		PVGL2_CVBO	21-47	123-139	PVMI_BEODV	280-297

PVG12_CVBF	123-139	174-180	284-279	PVMAT_CDOVO	146-166	
PVG12_CVMA	85-111	1267-1283		PVMAT_MEASI	87-104	
PVG12_CVMA6	85-111	1216-1231		PVMF_CAMVC	147-164	
PVG12_CVMJH	95-111	1126-1142		PVMF_CAMVD	147-164	
PVG12_CVPF9	442-467	800-816	1274-1260	PVMF_CAMVE	147-164	
PVG12_CVPPU	440-465	504-519	788-814	1272-1288	PVMF_CAMVF	147-164
PVG12_CVPRB	2116-233	676-592	1050-1088	PVMF_CAMVS	147-164	
PVG12_CVPRM	2118-233	576-592	1050-1088	PVMF_CAMVV	147-164	
PVG12_FIPV	803-819	1277-1283		PVMFA_HPBVO	11-84	
PVG12_IBV6	1058-1071			PVMFA_HPBV2	185-202	
PVG12_IBV8	1065-1070			PVMFA_HPBV4	185-202	
PVG12_IBVD2	1058-1071			PVMFA_HPBVA	174-191	
PVG12_IBVK	1055-1070			PVMFA_HPBVD	11-84	
PVG12_ISVH	701-716			PVMFA_HPBVJ	174-191	
PVG12_PRVIF	203-218			PVMFA_HPBVL	174-191	
PVG12_VZD	622-538			PVMFA_HPBVN	11-84	
PVG1C_HBVBC	476-480			PVMFA_HPBVO	174-191	
PVG1C_HSVE4	444-469			PVMFA_HPBVP	185-202	
PVG1C_HSVEB	427-442			PVMFA_HPBVS	11-94	
PVG1C_PRVIF	448-461			PVMFA_HPBVW	174-191	
PVG1C_VZD	160-188			PVMFA_HPBVY	174-191	
PVG1C_VZ18	150-188			PVMFA_HPBVZ	174-191	
PVG1D_HSIV1	78-84			PVMT2_JAANN	25-42	
PVG1D_HSIV2	79-84			PVMT2_JABAN	25-42	
PVG1E_PRVRI	3-94			PVMT2_IAPCW	25-42	
PVG1F_BRSVA	205-221	265-280		PVMT2_IAPFR	25-42	
PVG1F_BRBVC	205-221	265-280		PVMT2_IAPFW	25-42	
PVG1F_BRBVR	205-221	265-280		PVMT2_IALE1	25-42	
PVG1F_COVO	388-414			PVMT2_IALE2	25-42	
PVG1F_HRBV1	205-221	265-280		PVMT2_JAMAN	25-42	
PVG1F_HRBVA	205-221	265-280		PVMT2_JAPUE	25-42	
PVG1F_HRSVL	205-221	265-280		PVMT2_JASIN	25-42	
PVG1F_HRBVR	205-221	265-280		PVMT2_JAUDIO	25-42	
PVG1F_MEABE	286-302			PVMT2_JAWIL	25-42	
PVG1F_MEASI	289-305					
PVG1F_MEABY	288-302					
PVG1F_MUMPM						
PVG1F_MUMPR						
PVG1F_MUMPS						
PVG1F_INDVA						
PVG1F_INDVB						
PVG1F_INDYM						
PVG1F_INDVT						
PVG1F_INDVU						
PVG1F_PHODV						

PVGIF RINDK	282-398
PVGIF RINDL	282-298
PVGIF TATV	178-181
PVALI VZVD	279-293
PVGIM HANTB	356-371
PVGIM HANTH	499-518
PVGIM HANTL	499-515
PVGIM HANTY	499-515
PVGIM PTPV	743-758
PVGIM PUJNHH	609-626
PVGIM PUJUNS	609-626
PVGIM SECOUR	366-371
PVGIM SECOURS	366-371
PVGIM UJK	826-842
PVGIP BEV	889-895
PVGLY LA88Q	12-94
PVGLY LA89J	12-94
PVGLY LYCVIA	12-94
PVGLY LYCVW	12-94
PVGLY MOPEI	12-94
PVGLY PIARY	12-94
PVGNM CPMV	1021-1037
PVMAT REOVO	521-539
PVMAT NUMPS	191-207
PVMAT NDVA	136-161
PVMAT NDVB	136-161
PVMAT PI2HT	189-205
PVMAT 8V41	189-205
PVMAT 8V6	98-114
PVMP CAMVC	118-134
PVMP CAMVD	118-134
PVMP CAMVE	118-134
PVMP CAMVN	118-134
PVMP CAMVB	118-134
PVMP CAMVW	118-134
PVMP FAVD	116-131
PVMSA HPBG9	380-396
PVMSA HPBV9	187-202
PVMSA WHV1	378-383
PVMSA WHV58	383-388
PVMSA WHV7	383-398
PVMSA WHV18	383-398
PVMSA WHV81	383-398
PVMSA WHVV8	234-249
PVMT2 IAANN	28-40
PVMT2 IABAN	28-40
PVNT2 IAPOW	28-40

PVNT2	IAFPR	25-40
PVNT2	IAFPW	25-40
PVNT2	IALE1	25-40
PVNT2	IALE2	25-40
PVNT2	IAMAN	25-40
PVNT2	IAPUE	25-40
PVNT2	IABIN	25-40
PVNT2	IAUDO	25-40
PVNT2	IAVIL	25-40
PVNT2	NYXVL	228-241

TABLE VII

Search Results Summary for P3CTLZIP, P4CTLZIP,
P5CTLZIP, and P6CTLZIP Motifs

P3CTLZP	P4CTLZP	P5CTLZP	P6CTLZP	P8CTLZP
LIBRARY FILE	LIBRARY FILE	LIBRARY FILE	LIBRARY FILE	LIBRARY FILE
PENV HV27 147-185	PENV1 FRFSV 380-388	PENV1 FRFSV 380-400	PENV BIV06 47-88	625-648
PENV CAEVG 810-828	PENV AVISU 88-117	PENV FRFSV 380-400	PENV BIV27 47-88	147-168 564-575
PENV CAEVG 808-826	PENV BIV27 147-188	PENV BAEVN 170-180	PENV FENV1 226-246	830-851
PENV HV28E 760-788	PENV HV1ZH 123-142	PENV FIVPE 781-801	PENV FLVCL 824-845	
PENV HV2D1 741-759	PENV HV2D2 8-28	PENV FIVT2 779-798	PENV FLVGL 447-468	805-826
PENV HV261 741-759	PENV HV28B 778-787	PENV FIVT2 780-800	PENV FLVLB 487-488	826-846
PENV HV2N2 742-780	PENV JSRV 541-560	PENV FLVGL 8-28	PENV FLVSA 444-455	822-823
PENV HV2R0 761-789	PENV RSVP 633-652	PENV FOAMV 285-276	PENV FOAMV 153-174	887-978
PENV HV2SB 743-761	PHEMA VACCC 173-182	PENV FSVGA 9-28	PENV FSVGA 467-488	826-846
PENV HV2ST 745-783	PHEMA VACCI 173-182	PENV HV1C4 428-448	PENV FB7GB 447-468	805-826
PENV JSRV 378-394	PHEMA VACCT 173-182	PENV HV2CA 760-770	PENV FSV9M 460-471	808-828
PHEMA P12H 118-138	PHEMA VACCV 173-182	PENV NLVFC 400-420	PENV FSV1T 487-488	
PHEMA P12HT 118-138	PENV BEV 62-81	PENV MMVFB 643-663	PENV GALV 52-73	518-540
PHEMA SV41 55-73	PENV MCV1 61-80	PENV MMVFG 643-663	PENV HV2RE 760-771	
PENV THOOV 473-491	PENV MCV2 61-80	PENV OMVVS 75-85	PENV HV2G1 741-762	
PVG16 BPP22 63-101	PV/FUS ORFN2 28-48	PENV RSVP 42-62	PENV HV2NZ 742-783	
PVG24 BPT4 116-133	PVG01 HSVEB 168-188	PENV SFV1 924-944	PENV HV2RT 761-772	
PVG38 HSVA 344-362	PVG01 VACCC 378-395	PENV SFV3L 921-941	PENV HV2ST 745-788	
PVG40 HSVA 14-32	PVG01 VACCV 315-334	PENV SIVM1 788-788	PENV MCFF 600-621	
PVG50 HSVA 5-94	PVG01 VARV 378-385	PENV SIVMK 785-785	PENV MCFF3 601-622	
PVG51 BPT4 63-81	PVG08 BPT4 627-646	PENV SIVNL 784-784	PENV MLVAV 630-651	
PVG51 HSVA 84-102	PVG10 HSIVI 35-54	PENV SIVS4 789-789	PENV MLVCB 626-648	
PVG65 HSVI 185-173	PVG11 HSIVI 103-122	PENV SIVSP 773-793	PENV MLVFS 639-680	
PVGf1 IBVB 27BB-2806	3374-3382 PVG1 BPPH2 31-50	PHEMA CDVO 493-513	PENV MLVFS 639-680	
PVGf2 CVH22 1063-1071	PVG1 SPV1R 659-678	PHEMA CVBLY 391-411	PENV MLVFP 639-680	
PVGf2 IBV8 1058-1074	PVG20 BPT4 231-250	PHEMA CVBM 391-411	PENV MLVHO 628-647	
PVGf2 IBVB 1065-1073	PVG32 VZVD 90-108	PHEMA CVBQ 391-411	PENV MLVKI 197-188	
PVGf2 IBVD2 1066-1074	PVG38 BPK3 132-151	PHEMA CVHOC 391-411	PENV MLVMO 628-650	
PVGf2 IBVK 1056-1073	PVG37 BPT2 18-38	PHEMA CVMA6 402-422	PENV MLVRD 624-646	
PVGf2 IBVM 1056-1073	PVG39 BPT4 19-38	PHEMA JACKO 61-101	PENV MLVRK 624-646	
PVGf2 HSVA 650-678	PVG39 HSIVI 103B-1057	PHEMA JADMA 81-101	PENV MSVFB 170-181	
PVGf3 HSVA 692-710	PVG41 HSIVI 62-81	PHEMA NUMPM 387-417	PENV RMCFV 603-624	
PVGf3 HSVA 684-902	PVG43 BPPF3 380-398	PHEMA NUMPR 387-417	PENV SFTV1 867-878	
PVGf3 ILTV6 740-768	PVG46 BPPF1 337-356	PHEMA NUMPS 387-417	PENV SFT3L 167-178 864-876	
PVGf3 ILTV8 750-788	PVG58 HSIVI 142-161	PHEMA PHODV 493-513	PENV SIVAI 437-466	
PVGf3 ILTVT 750-788	PVG61 HSIVI 117-136	PHEMA PIHW 322-342	PHEMA SIVAO 442-483	
PYBLIC VZWD 431-449	PVG61 HSIVI 318-337	PHEMA PI2H 13-33	PHEMA SIVAI 421-442	
PYBLIC VZVS 431-449	PVG67 HSIVI 1687-1806 2108-2127	PHEMA PI2HT 13-33	PENV SIVAT 435-466	
PYBLF PI3H4 2-94	PVG62 CVBF 891-1010	PHEMA RINDL 497-517	PENV SIVASV 412-63	
PYBLH HSVA 314-332	PVal2 CVBL9 891-1010	PHEMA SEND5 322-342	PHEMA CYMA6 402-423	
PYBLH HSVE4 814-932	PVG12 CVBLY 981-1010	PHEMA SENDF 322-342	PHEMA IADE1 286-287	
PYBLH HSVEB 807-925	PVG12 CVBM 981-1010	PHEMA SENDH 322-342	PHEMA NUMPM 226-246	
PYBLH HSVI 6-84	PVG12 CVBV 981-1010	PHEMA SENDJ 322-342	PHEMA NUMPR 226-246	
PYBRM BP4V 879-998	PVG12 CVBV 981-1010	PHEMA SENDZ 322-342	PHEMA NUMPS 226-246	
PYMO1 YACCC 134-162	177-186 PVG12 CVH22	1118-1134 PVENV LELY 27-47	148-188 PHEMA PHODV 213-234	

PVM01 VACCV	83-101	126-144	PVGL2 CVMA4	099-1018	PVENV THGIV	356-376	PHEMA PI2H	13-34		
PVM1 REOVD	227-246		PVGL2 CVMA6	047-988	PVG01 VACCC	28B-318	PHEMA PI2HT	13-34		
PVM1 REOVL	227-246		PVGL2 CVMJH	858-977	PVG01 YACCV	237-267	PHEMA SV6	7-28		
PVMAT HR5VA	44-82		PVGL2 CVPPS	04-83	1038-1067	PVG01 VARV	28B-318	PHEMA SV6CM	7-28	
PVMAT NDVA	180-208		PVGL2 CVPPU	04-83	1038-1066	PVG08 VACCC	31-61	PHEMA SV6CP	7-28	
PVMAT NDVB	180-208		PVGL2 CVPRB	814-833		PVG08 VARV	31-61	PHEMA SV6LN	7-28	
PVMAT CAMVC	183-201		PVGL2 CVPRM	814-833	PVG09 BPPF1	25-45	PVG01 HSVFB	189-180		
PVMP CAMVO	183-201		PVGL2 FIPV	1041-1080	PVG12 HSV11	161-171	PVG01 HSVI1	889-910		
PVMP CAMVE	183-201		PVGL2 IBV8	588-807	771-790	PVG22 HSV11	300-320	PVG23 HSV11	314-335	
PVMP CAMVN	183-201		PVGL2 IBV8	589-808	770-789	PVG38 HSV11	048-668	970-980	PVG37 BPOX2	65-86
PVMP CAMV8	183-201		PVGL2 IBVD2	688-807	771-780	PVG51 HSV11	28-49	PVG43 HSV11	167-178	
PVMP CAMVW	183-201		PVGL2 IBVK	588-808	770-789	PVG83 HSV11	328-358	PVG55 HSV11	28B-309	
PVMP FMVD	180-88		PVGL2 IBVW	587-808	770-789	PVG65 HSV11	117-137	PVG65 HSVBA	65-106	
PVGLB HCMVA		708-725	PVGL2 HSVBA		PVG74 HSVBA	124-144	PVG68 HSV11	1165-1178		
PVGLB HCMVT		707-728	PVGL2 BV8		PVG82 HSVBA	328-348	PVG68 HSVBA	288-287		
PVGLB HSV8U		117-138	PVGL2 IBV8		PVG82 HSV11	327-347	PVG80 HSV11	30-51		
PVGLB LTV6		256-276	PVGL2 IBVD2		PVG82 HSV11	328-348	PVG83 HSV11	238-269		
PVGLB LTV8		268-285	PVGL2 IBVD3		PVG82 HSV11	328-348	PVG81 IBV8	1858-1877		
PVGLB LTVT		288-285	PVGL2 IBV8		PVG82 HSV11	327-347	PVG93 HCMVA	167-178		
PVGLC HSV11	3-84	487-486	PVGL2 IBV8		PVG82 CVBF	1268-1280	PVG82 CVBF	1268-1280		
PVGLC HSV1K	3-84	487-486	PVGL2 IBVU2		PVG82 CVBL9	1268-1280	PVG82 CVBL9	1268-1280		
PVGLC HSVBC	475-494		PVGLB EBV		PVG82 CVBLY	1268-1280	PVG82 CVBLY	1268-1280		
PVGLQ CHAV	436-455		PVGLB HCMVA		PVG82 CVBM	1268-1280	PVG82 CVBM	1268-1280		
PVGLQ RABVH	372-381		PVGLB HCMV7		PVG82 CVBQ	1268-1280	PVG82 CVBQ	1268-1280		
PVGLI HSVEB	44-63		PVGLB HSV23		PVG82 CVBV	1268-1280	PVG82 CVBV	1268-1280		
PVGLI VZVO	278-297		PVGLB HSV2H		PVG82 CVM4	1317-1339	PVG82 CVM4	1317-1339		
PVGLM BUNQE	117-136		PVGLB HSV28		PVG82 CVM5	1285-1288	PVG82 CVM5	1285-1288		
PVGLM PHV	182-171		PVGLB HSV6U		PVG82 CVMJH	1178-1187	PVG82 CVMJH	1178-1187		
PVGLM PTBV	897-1010		PVGLB HSV82		PVG82 HSV11	83-104	PVG82 HSV11	83-104		
PVGLM PUIMH	166-174		PVGLB HSV8A		PVG82 HSVIF	92-103	PVG82 HSVIF	92-103		
PVGLM PUUNS	166-174		PVGLB MCNV8		PVG82 HSVK	87-103	PVG82 HSVK	87-103		
PVGLA RVEV	830-849		PVGLF PI3H4		PVG82 HSVIP	83-104	PVG82 HSVIP	83-104		
PVGLM RVEVZ	830-849		PVGLG RABVE		PVG82 MCMVS	138-168	PVG82 MCMVS	138-168		
PVGLM UUK	658-674		PVGLG RABVH		PVG82 PRVIF	448-487	PVG82 PRVIF	448-487		
PVGLY LYCVW	89-108		PVGLG RABVP		PVG82 COVO	338-357	PVG82 COVO	338-357		
PVGNB CPMV	1166-1184		PVGLG RABVS		PVG82 MEABE	224-245	PVG82 MEABE	224-245		
PVM3 REOVD	621-640		PVGLG RABVT		PVG82 MEASJ	227-248	PVG82 MEASJ	227-248		
PVME1 CVBM	121-180		PVGLH MCNV8		PVG82 MEASY	224-245	PVG82 MEASY	224-245		
PVME1 CVH22	136-166		PVGLM BUNL7		PVG82 MUMPM	448-487	PVG82 MUMPM	448-487		
PVME1 CVPPB	174-183		PVGLM BUNBH		PVG82 MUMPR	448-487	PVG82 MUMPR	448-487		
PVME1 CVPPU	174-193		PVGLM BUNYY		PVG82 MUMPS	448-487	PVG82 MUMPS	448-487		
PVME1 CVPRM	174-193		PVGLM HANTB		PVG82 PHODV	306-326	PVG82 PHODV	306-326		
PVME1 CVTRE	171-180		PVGLM HANTH		PVG82 PH1HC	458-477	PVG82 PH1HC	458-477		
			PVGLM HANTL		PVG82 PI2H	450-471	PVG82 PI2H	450-471		
			PVGLM HANTV		PVG82 PI2HG	450-471	PVG82 PI2HG	450-471		
			PVGLM RVFVZ		PVG82 PI2HT	450-471	PVG82 PI2HT	450-471		
			PVGLM SEOUR		PVG82 PI3B	405-428	PVG82 PI3B	405-428		

PVGLM SEQ09	999-1010	PVGLF P13H4	483-474
PVGLM UUK	826-846	PVGLF RINDK	220-241
PVGLY LYCAV	12-32	PVGLP RINDL	220-241
PVGLY LYCW	12-32	PVGLP SENDS	480-481
PVGLY PIARY	12-32	PVGLF SENDF	480-481
PVGNB CPAYV	141-161	PVGLP SENDH	480-481
PVMMAT MUMPS	310-330	PVGLF SENDJ	480-481
PVMMAT NDVA	308-328	PVGLP SENDZ	480-481
PVMMAT NDVB	309-328	PVGLF SV41	483-474
PVMMAT P12HT	309-328	PVGLF SW6	448-467
PVMMAT PI4HA	312-332	PVGLH KOMYA	891-712
PVMMAT PI4HB	312-332	PVGLH HCMYT	890-711
PVMMAT SV41	308-328	PVGLH HSVE4	304-325
PVMMAT SV6	308-328	PVGLI HSVEB	297-318
PVME1 IBV6	74-94	PVGLI HSV7A	658-679
PVME1 IBVB	74-94	PVGLI HSV2	2-23
PVME1 IBVB2	74-94	PVGLI HSV23	2-23
PVME1 IBVK	74-94	PVGLM BUNGE	197-218
PVMIA HPBD8	201-221	PVGLM BUNL7	180-211
PVMIA HPBGS	208-228	PVGLM BUNSH	180-211
PVMIA HPBHE	283-313	PVGLM BUNYW	183-214
PVMIA WHV1	207-227	PVGLY LAB6G	237-258
PVMIA WHV5B	212-232	PVGLY LAS8J	238-259
PVMIA WHY7	212-232	PVGPB EBV	67-88
PVMIA WHV8	212-232	PVM01 VACCC	281-302
PVMIA WHVBI	212-232	PVM01 VACCV	230-251
PVMIA WHVW8	63-83	PVMAT HRSVA	188-180
		PVMAT RINDK	200-221
		PVMAT TATV	122-143
		PVME1 CYHOC	64-85
		PVMBA HPBDB	201-222
		PVMBA HPBVO	70-91
		PVMBA HPBV2	244-265
		PVMBA HPBV4	244-265
		PVMBA HPBV9	244-265
		PVMBA HPBVA	233-264
		PVMBA HPBVD	70-91
		PVMBA HPBVI	233-264
		PVMBA HPBVJ	233-264
		PVMBA HPBVL	233-264
		PVMBA HPBVN	70-91
		PVMBA HPBVO	233-264
		PVMBA HPBVP	244-288
		PVMBA HPBVR	244-288
		PVMBA HPBVS	70-91
		PVMBA HPBUW	233-264
		PVMBA HPBVY	233-264

PVMSA_HPBVZ	233-264
PVMT2_IAMAN	25-46
PVMT2_IABAN	26-46
PVMT2_IAFOW	25-46
PVMT2_IAPFR	25-46
PVMT2_IAPFW	26-46
PVMT2_IALE1	25-46
PVMT2_IALE2	25-46
PVMT2_IAMAN	25-46
PVMT2_IAPUE	25-46
PVMT2_IASIN	26-46
PVMT2_IAUDIO	26-46
PVMT2_IAWIL	26-46

TABLE VIII

**Search Results Summary for P7CTLZIP,
P8CTLZIP, and P9CTLZIP Motifs**

PCTZIP	PCTZIP	PCTZIP	PCTZIP
LIBRARY FILE	LIBRARY FILE	LIBRARY FILE	LIBRARY FILE
PENV_BAEVM	202-224	PENV_FRSFV	380-403
PENV_HV1B1	48B-620	PENV_BLVAF	380-403
PENV_HV1B8	483-516	PENV_BLVAV	303-327
PENV_HV1BN	494-616	PENV_BIV06	178-201
PENV_HV1BR	603-626	PENV_BIV27	207-230
PENV_HV1EL	495-617	PENV_FOAMV	684-887
PENV_HV1H2	498-620	PENV_HV1Z3	176-189
PENV_HV1H3	498-620	PENV_HV2BE	3-26
PENV_HV1J3	610-532	PENV_HV2CA	750-773
PENV_HV1JR	480-612	PENV_HV2DI	3-26
PENV_HV1KB	604-626	PENV_HV2G1	772-785
PENV_HV1MA	600-522	PENV_HV2NZ	777-800
PENV_HV1MF	488-518	PENV_JSRV	641-684
PENV_HV1ND	488-510	PENV_SFV1	864-887
PENV_HV1PV	498-520	PENV_SFV3L	861-884
PENV_HV1S1	489-611	PENV_SIVM1	803-826
PENV_HV1Z2	123-146	PENV_SIVMK	802-825
PENV_HV1Z8	497-519	PENV_SIVML	601-824
PENV_HV2Z9	506-527	PENV_SIVSA	808-829
PENV_HV2ZH	488-620	PENV_SIVSP	810-833
PENV_JSRV	316-398	PHEMA_COVO	200-223
PENV_MPMV	213-236	PHEMA_P12H	65-88
PENV_SRV1	213-236	PHEMA_P12T	65-88
PHEMA_IAC	37-69	PVF11_VACCC	161-184
PHEMA_IABN	21-43	PVF15_VACCC	25-48
PHEMA_IADA3	37-69	PVF16_VACCP	3-26
PHEMA_IADH2	21-43	PVF11_AMEPV	313-336
PHEMA_IADH3	21-43	PVF29_HSVI1	461-514
PHEMA_IADH4	21-43	PVF33_HSVI1	322-346
PHEMA_IADH5	21-43	PVF32_HSVI1	229-262
PHEMA_IADH6	21-43	PVF37_HSVI1	722-745
PHEMA_IADH8	21-43	PVF32_CVBF	10-33
PHEMA_IADH7	21-43	PVF39_HSVI1	661-674
PHEMA_IADM2	37-69	PVF12_CVBL9	10-33
PHEMA_IADM4	29-60	PVF12_CVBL2	1267-1280
PHEMA_IADM3	37-69	PVF12_CVMA6	1216-1238
PHEMA_IENB8	21-43	PVF12_CVMAJH	1126-1149
PHEMA_IEN7	37-69	PVF12_CVPFS	1274-1287
PHEMA_IAMAO	37-69	PVF12_CVPPU	1272-1295
PHEMA_IAME1	37-69	PVF12_CVPR8	1050-1073
PHEMA_IAME2	37-69	PVF12_CVPRM	1050-1073
PHEMA_IAME6	21-43	PVF12_FIPV	1277-1300
PHEMA_IANT6	37-68	PVF12_IBV6	196-219
PHEMA_IACU7	21-43	PVF12_IBVB	196-218
PHEMA_IATK8	33-66	PVF12_IBVD2	196-219
PHEMA_IAUO	37-69	PVF12_IBVD3	196-219

PHEMA_IAV17	38-60	PVAL2_IBVK	196-218	PV3IB HSVMD	688-813
PHEMA_IAX31	37-59	PVAL2_IBVM	198-218	PVALB_LTV6	687-821
PHEMA_IA2CO	37-58	PVAL2_IBVU1	178-201	PVALB_LTV8	687-831
PHEMA_JAZH2	21-43	PVAL2_IBVU2	178-201	PVALB_LTV7	687-831
PHEMA_IAZH3	21-43	PVAL2_IBVU3	178-201	PVGL H6V11	413-427
PHEMA_JAZUK	37-58	PVALB_HCMVA	635-558	PVGLF_VZVD	480-483
PHEMA_PHODV	36-56	PVALB_HCMVT	638-659	PVGLF_SVG	401-426
PHEMA_P12H	65-87	PVALB_HSVBA	493-606	PVALH_HCMVA	674-589
PHEMA_P12H	65-87	PVALB_HMCV8	599-589	PVALH_HCMVT	673-587
PVFPT7_CAFYK	89-111	PVALC_HSV11	487-480	PVALH_HSV11	443-487
PVFUS_VACC8	72-84	PVGLC_H9V1K	487-480	PVALH_HSV1E	443-467
PVG01_HSVII	317-338	PVALC_HSV2	435-468	PVALM_BUNL7	31-56
PVG03_VACCC	60-72	PVALC_HSV23	438-469	PVALM_BUNSH	31-56
PVG03_VARV	60-72	PVALM_BUNL7	1387-1410	PVALM_RVTH	684-719
PVG04_VACC	11-33	PVALM_BUNSH	1387-1410	PVALM_RVFV	344-368
PVG04_VARV	11-33	PVALM_UUK	668-688	PVALM_RVFV2	344-368
PVG19_HSVII	68-110	PVGLY_JUNIN	12-36	PVALM_UUK	681-686
PVG28_HSVII	173-186	PVGLY_LASBG	12-35	PVANM_CPMV	311-335
PVG30_HSVII	20-42	PVGLY_LASBJ	12-35	PVG32_EBV	667-681
PVG46_HSVII	134-166	PVGLY_LYCV	12-35	PVdP3_EBV	654-678
PVG48_HAVSA	71-93	PVGLY_LYCVW	12-35	PVM1_RECVD	280-304
PVG66_HAV6A	208-298	PVGLY_M0PEI	12-35	PVM1_RECVL	280-304
PVG69_HSVII	267-288	PVGLY_TACV	12-35	PVM2_RECVD	188-192
PVG69_SPV7A	142-64	PVGLY_TACVS	12-35	PVM22_RECVD	168-182
PVG80_HSVII	63-76	PVGLY_TACY7	12-35	PVM2_RECVJ	168-182
PVG85_HSVII	1347-1369	PVGLY_TACVT	12-35	PVM2_RECVL	168-182
PVG86_HAV6A	60-82	PVGMN_CPMV	741-784	PVMMAT_MEASI	87-111
PVG86_SPVIR		PVMM1_RECVD	324-347	PVMMAT_BSPVIB	314-339
PVG12_IBV6	1068-1078	PVMM1_RECVL	464-477	PVME1_CVBM	137-161
PVG12_IBV8	1068-1077	PVMMAT_MUMPS	227-250	PVME1_CVHOC	137-161
PVG12_IBV12	1068-1078	PVMSA_HPBDB	269-292	PVME1_CVTKE	137-161
PVG12_IBVK	1068-1077	PVMSA_HPDIC	269-291	PVME1_IBV6	74-98
PVG12_IBVM	1085-1077	PVMSA_HPADU	231-264	PVME1_IBV	74-98
PVG12_HBV6U	117-138	PVMSA_HPBDW	269-292	PVME1_IBVB2	74-98
PVG12_HBV8	745-787	PVMSA_HPBHE	238-269	PVME1_IBVK	74-98
PVALC_HAV8B	309-421	PVMSA_HBVMM		PVMSA_HPBGB	271-285
PVALC_HBVMM	308-420	PVMSA_WHV1		PVMSA_WHV6	269-283
PVALC_HBVMM	309-421	PVMSA_WHV6		PVMSA_WHV6	126-149
PVALF_BR8VA	265-287	482-604		PVMSA_WHV6B	274-288
PVALF_BR8VC	484-506			PVMSA_WHV7	274-288
PVALF_BR8VR	484-506			PVMSA_WHV8	274-288
PVALF_BR8V1	484-506			PVMSA_WHV8I	274-288
PVALF_HBVVA	484-506			PVMSA_WHV8I	274-288
PVALF_HBSVL	484-506			PVMSA_WHV8I	274-288
PVALF_HBSVR	484-506			PVMSA_WHV8I	274-288
PVALF_TRTV	482-474			PVMSA_WHV8I	274-288
PVALG_HNV	77-99			PVMSA_WHV8I	274-288
PVALG_WH8VO	408-428			PVMSA_WHV8I	274-288

PVALH HSVE4	814-838
PVALH HSVEB	807-828
PVALI HCAVA	188-180
PVGLM PTPV	743-765
PVALP BEV	430-482
PVALY LASQ	428-448
PVALY LASJ	427-449
PVALY MOPEI	426-447
PVGCP2 EAV	857-879
PVGCP3 EAV	856-876
PVM1 REOVD	414-436
PVM1 REQVL	414-438
PVM3 REQVD	304-326
PVMAT PIHC	195-217
PVMAT PIHT	192-154
PVMAT SENDF	195-217
PVMAT SENDH	195-217
PVMAT SENDZ	195-217
PVMAT SV41	132-184
PVMEM EBV	131-153
PVMP CERV	283-315

TABLE IX

Search Results Summary for P12CTLZIP Motif

PENV HV1ZH	123-142	438-453	489-520
PENV HV2BE	3-26	750-775	781-804
PENV HV2CA	760-777		
PENV HV2D1	3-26	741-768	772-785
PENV HV2D2	9-28		
PENV HV2G1	741-766	772-795	
PENV HV2N2	742-767	777-800	
PENV HV2R0	761-776		
PENV HV2B8	713-768	778-804	
PENV HV2ST	745-770		
PENV JSRV	104-119	289-325	376-398
PENV MCFF	600-621		
PENV MCF3	801-822		
PENV MLVAV	630-651		
PENV MLVCB	628-644		
PENV MLVFS	639-660		
PENV MLVFF	639-660		
PENV MLVFP	639-660		
PENV MLVHO	626-647		
PENV MLVKI	187-188		
PENV MLVMO	626-660		
PENV MLVTD	624-645		
PENV MLVRK	624-645		
PENV MMTRB	643-663		
PENV MMTVG	643-663		
PENV MPMV	213-235		
PENV MSVFB	170-191		
PENV OMVVB	75-100	658-683	
PENV RMCFV	603-624		
PENV RSVP	42-69	653-652	
PENV SFV1	300-325	710-727	864-887
PENV SFV2L	167-178	304-329	707-724
PENV SIVAI	437-469		
PENV SIVAG	442-463		
PENV SIVAI	421-442		
PENV SIVAT	436-458		
PENV SIVGB	93-109		
PENV SIVM1	766-783	803-826	
PENV SIVM2	138-184	768-792	802-826
PENV SIVMK	138-154	784-791	801-824
PENV SIVML	769-789	808-829	
PENV SIVS4	773-783	810-833	
PENV SIVSAV	42-63		
PENV SRV1	213-235		
PHEMA COVO	36-53	200-223	
PHEMA CVBLY	391-415		
PHEMA CVBM	391-415		

PHEMA CVBQ	391-418
PHEMA CVHOC	391-418
PHEMA CVMG	402-423
PHEMA CVMS	403-418
PHEMA IAAIC	37-69
PHEMA IABAN	21-43
PHEMA IABUD	320-337
PHEMA JACKA	320-337
PHEMA JACKY	230-246
PHEMA JACKG	81-101
PHEMA JACKQ	302-319
PHEMA JACKQ	302-319
PHEMA JACKS	319-336
PHEMA JACSY	320-337
PHEMA JADAI	320-337
PHEMA JADA2	318-336
PHEMA JADA3	37-58
PHEMA JADC2	320-337
PHEMA JADE1	286-287
PHEMA JADH1	306-323
PHEMA JADH2	21-43
PHEMA JADH3	21-43
PHEMA JADH4	21-43
PHEMA JADIE	21-43
PHEMA JADIG	21-43
PHEMA JADH7	21-43
PHEMA JADM2	37-58
PHEMA JADMA	28-59
PHEMA JADN2	320-337
PHEMA JADU3	37-59
PHEMA IAENG	21-43
PHEMA IAEN7	37-69
PHEMA JAFFR	230-246
PHEMA IAGRE	320-337
PHEMA IAGU2	320-337
PHEMA IAGUA	319-336
PHEMA IAHAL	321-338
PHEMA IAHAR	230-246
PHEMA IAHCO	230-246
PHEMA IAHCT7	230-246
PHEMA IAHCO	230-246
PHEMA IAHDE	230-246
PHEMA IAHFO	236-252
PHEMA IAHKG	321-338
PHEMA IAHK7	236-252
PHEMA IAHLE	230-246
PHEMA IAHLO	236-252
PHEMA IAHMI	236-252

PHEMA JAHNM	239-252	321-338
PHEMA JAHNN	316-332	
PHEMA JAHPR	316-332	
PHEMA JAHO	236-252	321-338
PHEMA JAHS	236-252	321-338
PHEMA JAHSR	230-246	316-332
PHEMA JAHSW	230-246	316-332
PHEMA JAHTE	236-252	321-338
PHEMA JAHTO	236-252	321-338
PHEMA JAHTUR	236-252	321-338
PHEMA JAJAP	317-334	
PHEMA JAMAA	187-223	318-338
PHEMA JAMAB	202-248	324-341
PHEMA JAMAO	37-59	312-339
PHEMA JAME1	37-59	322-339
PHEMA JAME2	37-59	322-339
PHEMA JAME6	21-43	
PHEMA JAMIN	85-101	231-247
PHEMA JANTO	37-59	322-339
PHEMA JAPIL	320-337	
PHEMA JAQU7	21-43	308-333
PHEMA JARUD	320-337	
PHEMA JA8E2	320-337	
PHEMA JA8H2	321-338	
PHEMA JASTA	230-246	316-332
PHEMA JATAI	323-55	320-337
PHEMA JATKI	233-249	
PHEMA JATKR	230-246	
PHEMA JATKV	239-246	
PHEMA JAUDO	37-59	322-339
PHEMA JAV7	38-59	323-340
PHEMA JAX31	37-59	
PHEMA JAZCO	37-59	322-339
PHEMA JAZH2	21-43	306-333
PHEMA JAZH3	21-43	308-333
PHEMA JAZUK	37-59	322-339
PHEMA INBAA	116-131	286-310
PHEMA INBBE	123-139	203-318
PHEMA INBBO	116-132	283-308
PHEMA INBEN	123-138	301-318
PHEMA INBFU	108-124	286-301
PHEMA INBGL	119-135	296-311
PHEMA INBHK	116-132	293-308
PHEMA INBIB	108-124	289-303
PHEMA INBID	120-136	299-314
PHEMA INBLE	123-139	302-317
PHEMA INBMD	113-129	292-307

PHEMA INBME	116-132	288-311
PHEMA INBNA	106-124	288-303
PHEMA INBOR	123-139	301-316
PHEMA INBSI	123-138	301-316
PHEMA INBSJ	116-135	288-313
PHEMA INBUS	116-132	284-309
PHEMA INBVI	116-132	286-311
PHEMA INBYK	123-139	303-318
PHEMA INBYB	108-124	288-301
PHEMA INCCA	442-466	
PHEMA INCEN	430-464	
PHEMA INCOL	430-454	
PHEMA INCY	428-463	
PHEMA INCJH	443-467	
PHEMA INCCY	428-453	
PHEMA INCMJ	428-453	
PHEMA INCNM	428-453	
PHEMA INCNA	428-483	
PHEMA INCPI	430-454	
PHEMA INCP2	430-464	
PHEMA INCP3	430-464	
PHEMA INCTA	430-464	
PHEMA INCYA	430-464	
PHEMA MUMPM	133-148	226-246
PHEMA MUMPR	101-125	133-148
PHEMA MUMPS	101-125	133-148
PHEMA NDVA	93-110	
PHEMA NDVB	93-110	
PHEMA NDVO	93-110	
PHEMA NDVH	93-110	
PHEMA NDVI	93-110	
PHEMA NDVM	93-110	
PHEMA NDVQ	93-110	
PHEMA NDVQ	93-110	
PHEMA NDVU	93-110	
PHEMA PHODV	38-58	213-234
PHEMA PI1HW	28-53	322-342
PHEMA PI2H	13-40	05-89
PHEMA PI2HT	13-40	05-89
PHEMA PI3B	111-128	272-299
PHEMA PI3H4	111-128	324-340
PHEMA PI3HA	111-128	324-340
PHEMA PI3HT	111-128	322-340
PHEMA PISHU	111-128	272-299
PHEMA PI3HV	111-128	324-340
PHEMA PI3HV	111-128	272-299
PHEMA PI3HX	111-128	324-340
PHEMA PI4HA	60-67	

PHEMA RINDK	368-363	
PHEMA RINDL	4-30	
PHEMA SENDS	322-342	
PHEMA SENDF	322-342	
PHEMA SENDH	322-342	
PHEMA SENDJ	322-342	
PHEMA SENDZ	322-342	
PHEMA SV41	65-73	65-102
PHEMA SV5	7-28	84-101
PHEMA SVRCM	7-28	84-101
PHEMA SVSCP	7-28	84-101
PHEMA SVSN	7-28	84-101
PHEMA VACCC	173-192	
PHEMA VACCI	173-192	
PHEMA VACCT	173-192	
PHEMA VACCV	173-192	
PVENV BEV	92-98	87-114
PVENV DHV1	42-67	48A-611
PVENV EAV	26-41	
PVENV LEV	27-47	14B-168
PVENV MCV1	01-80	
PVENV MCV2	01-80	308-333
PVENV THGIV	186-221	356-383
PVF05 VACCC	280-305	
PVF05 VACCP	280-305	
PVF05 VACCV	280-305	
PVF09 VACCC	176-200	
PVF09 VACCV	176-200	
PVF11 VACCC	181-184	
PVF16 VACCC	25-48	
PVF16 VACCP	3-28	
PVFP1 FOWPV	287-323	
PVFP2 FOWPV	88-104	
PVFP7 CAPVK	88-111	
PVFP7 FOWPV	85-90	
PVFP8 CAPVK	61-76	
PVFS8 ORENZ	28-48	
PVFS8 VACCE	72-98	
PVFS8 VACCV	189-196	
PVGO1 HSVB	210-226	317-359
PVGO1 HSVI1		638-616
PVGO1 VACCC	288-316	376-395
PVGO1 VACCV	237-257	315-334
PVGO1 VARV	308-316	376-395
PVGO1 YZVD	68-82	
PVGO3 VACCC	60-72	
PVGO3 VARV	60-72	
PVGD4 VACCC	11-33	

PVG04 VARV	11-33
PVG06 VACCC	31-51
PVG08 VARV	31-51
PVG09 HSVII	134-148
PVG10 HSVII	36-54
PVG10 HSVBA	108-124
PVG11 HSVI	103-122
PVG12 HSVII	151-178
PVG12 HSVBA	88-92
PVG15 HSVEB	184-209
PVG16 HSVII	88-112
PVG17 HSVII	313-338
PVG1L AMEPV	
PVG1L SPVIR	78-92
PVG22 HSVII	300-317
PVG23 HSVII	314-335
PVG27 HSVII	158-184
PVG27 HSVBA	206-238
PVG28 HSVII	173-197
PVG28 HSVBA	14-40
PVG38 HSVII	20-42
PVG30 HSVII	186-191
PVG32 VZV/D	90-109
PVG36 HSV9A	108-123
PVG37 HSVII	284-299
PVG39 HSVII	649-675
PVG40 HSVII	14-32
PVG41 HSVII	11-38
PVG43 HSVII	109-133
PVG46 HSVII	134-159
PVG48 HSVBA	71-93
PVG50 HSVII	6-30
PVG50 HBVBA	63-81
PVG61 HSVII	29-49
PVG62 HSVII	229-252
PVG66 HSVII	22-37
PVG66 HSVBA	65-106
PVG69 HSVII	1185-1176
PVG69 HSVBA	130-148
PVG69 HSVII	142-161
PVG69 SPVA	42-64
PVG80 HSVII	30-81
PVG81 HSVII	79-102
PVG83 HSVII	238-259
PVG84 HSVII	420-445
PVG85 HSVII	117-137
PVG87 HSVII	108-132
PVG8 SPVIR	60-82

PVGLB HSVEA	736-763
PVGLB HSVEB	736-763
PVGLB HSVEL	736-753
PVGLB HSVMD	688-613
PVGLB HSVSA	483-508
PVGLB ILTV6	269-276
PVGLB ILTV9	268-288
PVGLB ILTVT	288-295
PVGLB MCNVS	135-169
PVGLC PRVIF	203-218
PVGLB VZD	622-538
PVGLC HSV11	487-493
PVGLC HSV1K	3-22
PVGLC HSV2	435-458
PVGLC HSV23	439-459
PVGLC HSVBC	476-484
PVGLC HAVE4	444-459
PVGLC HSVFB	427-442
PVGLC HSVMB	389-421
PVGLC HSVMA	389-420
PVGLC HSVMM	389-421
PVGLC PRVTE	180-197
PVGLC VZD	431-449
PVGLC VZI8	431-449
PVGLD HSV11	79-84
PVGLD HBV2	79-84
PVGLE HSV11	104-129
PVGL E ZVD	469-493
PVGLF BRSVA	206-221
PVGLF BRSVC	205-221
PVGLF BRSVR	205-221
PVGLF COVO	336-381
PVGLF HRSVI	205-221
PVGLF HRSVA	205-221
PVGLF HRSVL	206-221
PVGLF HRSVR	205-221
PVGLF MEASE	224-246
PVGLF MEABI	227-249
PVGLF MEASY	224-248
PVGLF MUMPM	218-292
PVGLF MUMPR	218-292
PVGLF MUMPS	5-20
PVGLF NDVA	213-289
PVGLF NDVB	213-289
PVGLF NDVM	213-289
PVGLF NDVT	213-289
PVGLF NDVTG	213-289

PVGLF NDVU	273-289			
PVGLF PHODY	269-285	308-326	387-393	631-658
PVGLF P11HC	458-477			
PVGLF P12H	450-471			
PVGLF P12HQ	450-471			
PVGLF P12HT	450-471			
PVGLF P13B	203-310	405-426	453-474	
PVGLF P13H4	2-20	283-310	453-474	
PVGLF RINDK	220-241	282-298	447-472	
PVGLF RNDL	220-241	282-298	447-473	
PVGLF SEND6	450-481			
PVGLF SEND6F	450-481			
PVGLF SENDH	450-481			
PVGLF SENDJ	450-481			
PVGLF SENDZ	450-481			
PVGLF BV41	453-474			
PVGLF BV5	401-426	449-487		
PVGLF TRTV	176-191	452-474		
PVGLG BHNV	77-99			
PVGLG RABVE	454-474			
PVGLG RABVH	372-391	454-474		
PVGLG RABVP	454-474			
PVGLG RABV8	454-474			
PVGLG RABV7	454-474			
PVGLQ VH8Y0	408-428			
PVGLH HCMVA	211-237	385-382	574-608	691-712
PVGLH HCMNT	210-236	384-381	673-697	690-711
PVGLH HSV11	246-262	443-467	803-827	
PVGLH HSV1E	245-262	443-467	803-827	
PVGLH HSV8Q	314-332			
PVGLH HSV84	304-326	814-839		
PVGLH HSV8B	287-318	807-832		
PVGLH HSV8A	454-479	658-678		
PVGLH MCMVB	870-890			
PVGLI HCMVA	158-180			
PVGLI HAV11	43-60			
PVGLI HAEVB	44-69			
PVGLI VZVD	278-297			
PVGLM BUNGE	117-136	167-222		
PVGLM BUN7	31-56	81-98	180-211	1325-1345
PVGLM BUN8	31-56	81-98	180-211	1325-1345
PVGLM BUN9W	183-218	1378-1406		
PVGLM HANTB	366-371	692-717	800-816	698-7019
PVGLM HANTH	499-515	694-718	1000-1020	
PVGLM HANTL	499-515	694-718	1001-1021	
PVGLM HANTV	499-515	694-718	1001-1021	
PVGLM PHV	162-171			

PVALM_PTPV	743-7-65	887-1010	1276-1-302
PVALM_PUUMH	155-174	509-525	712-229
PVALM_PUUMS	155-174	509-525	712-729
PVALM_RVFV	63-80	344-388	830-858
PVALM_RVFVZ	63-80	344-398	830-858
PVALM_SEOUR	355-371	693-718	801-916
PVALM_SEOUS	356-371	692-717	800-916
PVALM_UJK	681-585	655-674	826-842
PVALP_BEV	430-452	669-695	1069-1-124
PVALX_PRVRI	148-176		1646-1568
PVGLY_JUNIN	12-38		
PVGLY_LASSE	12-38	237-268	426-448
PVGLY_LASBJ	12-38	238-269	427-449
PVGLY_LYCA	12-38		
PVGLY_LYCWV	12-38	69-108	
PVGLY_MOPEL	12-38	428-447	
PVGLY_PIARV	12-38	441-466	
PVGLY_TACV	12-38		
PVGLY_TACV6	12-38		
PVGLY_TACV7	12-38		
PVGLY_TACV7	12-38		
PVGNB_CPNMV	141-161	568-584	767-783
PVGRIM_BPMW	678-896		
PVGRIM_CPMV		311-336	741-784
PVGP2_EBV	887-891		1021-1-037
PVGP3_EBV	854-878		
PVG9_EBV	97-98		
PVM01_VACC	134-169	177-196	281-302
PVM01_VACCV	83-108	126-144	230-261
PVM1_RECVD	141-168	227-246	280-304
PVM1_RECVL	141-168	227-246	280-304
PVM21_RECVD	168-192		
PVM22_RECVD	168-192		
PVM2_RECVL	168-192		
PVM3_RECVD	304-328	621-640	
PVMAT_BRSA	217-62		
PVMAT_CDVO	148-165	203-309	
PVMAT_HRSVA	44-62	139-160	
PVMAT_LPMV	311-338		
PVMAT_MEASE	263-309		
PVMAT_MEASH	263-309		
PVMAT_MEASI	87-111		
PVMAT_MEASU	263-309		
PVMAT_HUMPS	161-207	227-250	310-320
PVMAT_NOVA	135-161	190-208	308-329
PVMAT_NDVB	135-161	180-208	308-329

PVMAT PI1HC	188-217		
PVMAT PI2HT	132-184	188-206	308-328
PVMAT PI4HA	312-332		
PVMAT PI4HB	312-332	288-280	288-309
PVMAT RINDX	200-221		
PVMAT BENDF	185-217		
PVMAT SENIDH	195-217		
PVMAT BENDZ	195-217		
PVMAT 88PV8	288-308	314-338	
PVMAT 8V41	132-154	188-205	308-328
PVMAT 8V6	98-114	132-148	308-336
PVMAT SVCV	141-157		
PVMAT TRDV	122-149		
PVME1 CVBM	9-38	137-161	171-180
PVME1 CVH22	136-155		
PVME1 CVPPLU	174-183		
PVME1 CVHOC	9-38	64-86	137-161
PVME1 CVMA5	10-37		
PVME1 CVMJH	10-37		
PVME1 CVPP8	174-193		
PVME1 CVPPLU			
PVME1 CVPRM	174-183		
PVMB1 CYTRE	9-39	137-161	171-180
PVME1 IBV6	74-86		
PVME1 IBV8	74-101		
PVME1 IBV2	74-101		
PVME1 IBVK	74-88		
PVMEM EBV	131-167	178-203	
PVNP CANYC	118-134	147-164	183-201
PVNP CAMVD	116-134	147-164	183-201
PVNP CANVE	118-134	147-164	183-201
PVNP CAMVN	116-134	147-164	183-201
PVNP CANVB	116-134	147-164	183-201
PVNP CAMWV	116-134	147-164	183-201
PVNP CERV	283-316		
PVNP FANV	116-131	180-188	
PVNP SOCHAV	122-147	273-299	
PVNSA HPB08	201-226	268-285	
PVNSA HPBDIC	184-221	268-294	
PVNSA HPBDU	187-184	231-257	
PVNSA HPBDW	184-221	269-295	
PVNSA HPB09	208-236	271-295	308-396
PVNSA HPBHE	238-262	283-320	
PVNSA HPBV0	70-69		
PVNSA HPBV2	185-202	244-270	
PVNSA HPBV4	186-202	244-270	
PVNSA HPBV9	244-270		
PVNSA HPBV4	174-191	233-259	

PVMSA_HPBVD	11-28	70-86
PVMSA_HPBVI	233-269	
PVMSA_HPBVJ	174-191	233-269
PVMSA_HPBVL	174-191	233-269
PVMSA_HPBVN	11-28	70-86
PVMSA_HPBVO	174-191	233-269
PVMSA_HPBVP	165-202	244-270
PVMSA_HPBVR	185-202	244-270
PVMSA_HPBVS	11-28	70-86
PVMSA_HPBWW	174-191	233-269
PVMSA_HPBYY	174-191	233-269
PVMSA_HPBYZ	174-191	233-269
PVMSA_WHV1	207-234	269-293
PVMSA_WHV1	212-239	274-288
PVMSA_WHV68	212-239	274-288
PVMSA_WHV7	212-239	274-288
PVMSA_WHV8	212-239	274-288
PVMSA_WHV81	212-239	274-288
PVMSA_WHVW6	125-149	234-249
PVMT2_JAANN	26-48	
PVMT2_JABAN	26-48	
PVMT2_JAFOW	26-48	
PVMT2_JAFFR	25-49	
PVMT2_JAFPN	28-49	
PVMT2_JALE1	28-48	
PVMT2_JALE2	25-49	
PVMT2_JAMAN	25-48	
PVMT2_JAPUE	25-48	
PVMT2_JASIN	25-48	
PVMT2_JAUDDO	26-48	
PVMT2_JAWIL	26-48	
PVMT2_MTYXVL	226-241	

TABLE X

Search Results Summary for P23CTLZIP Motif

P23ZIPC	LIBRARY FILE	
PENV AVISU	98-136	
PENV BAEVM	202-240	528-564
PENV BIV08	434-472	528-583
PENV BIV27	584-682	628-688
PENV CAEVQ	44-78	
PENV EIAYI	795-828	
PENV EIAY2	795-828	
PENV EIAY3	795-828	
PENV EIAY5	795-828	
PENV EIAY9	795-828	
PENV EIAYC	795-828	
PENV EIAYW	795-828	
PENV EIAYY	795-828	
PENV EIVPE	126-186	
PENV FIVT2	49-74	
PENV FIVVL	447-476	
PENV FIVLB	467-495	
PENV FIVBA	444-472	
PENV FOAMV	44-78	461-518
PENV FRFBF	316-390	662-584
PENV FB70A	467-495	
PENV FB70B	447-476	
PENV FB78M	460-479	
PENV FB78T	467-495	
PENV QALY	519-584	
PENV HV1A2	728-782	
PENV HV1B1	730-783	
PENV HV1BB	726-768	
PENV HV1BN	743-781	
PENV HV1BR	736-788	
PENV HV1C0	742-776	
PENV HV1EL	264-286	727-780
PENV HV1H2	730-783	
PENV HV1H3	730-783	
PENV HV1L3	741-774	
PENV HV1J0	722-766	
PENV HV1K9	652-680	762-780
PENV HV1MA	268-289	733-788
PENV HV1MF	728-781	
PENV HV1MN	382-430	731-784
PENV HV1ND	248-278	
PENV HV1OY	729-782	
PENV HV1PV	730-783	
PENV HV1RH	738-772	
PENV HV1SC	750-783	

PENV HV1W1	730-763
PENV HV1W2	721-764
PENV HV1Z2	264-265
PENV HV1Z3	260-281
PENV HV1Z6	266-288
PENV HV1Z8	265-289
PENV HV2B8	781-811
PENV HV2D1	772-802
PENV HV2G1	772-802
PENV HV2N2	777-814
PENV HV2S8	743-776
PENV HV3B1	288-322
PENV JSBV	484-616
PENV JMTV0	438-472
PENV JMTVQ	436-472
PENV RSVP	633-670
PENV SIVF1	44-78
PENV SIVF3L	48-82
PENV SIVCZ	745-778
PENV SIVGB	247-277
PENV SIVM1	768-800
PENV SIVMK	768-798
PENV SIVML	611-645
PENV SIV84	468-486
PENV SIVSP	432-490
PHEMA COVO	200-234
PHEMA IABUD	23-55
PHEMA JACKA	23-56
PHEMA JACKY	617-647
PHEMA JADA1	23-66
PHEMA JACZ	23-55
PHEMA JADH6	293-323.
PHEMA JADN2	23-66
PHEMA JAPR	16-61
PHEMA JAGRE	23-65
PHEMA JAMAA	22-64
PHEMA JAMAB	27-69
PHEMA JARUD	23-65
PHEMA JASE2	23-66
PHEMA JASTA	617-647
PHEMA MUMPM	19-62
PHEMA MUMPR	19-62
PHEMA MUMPS	19-62
PHEMA NDVA	60-68
PHEMA NDVB	60-68
PHEMA NDVD	60-68
PHEMA NDVH	60-68
PHEMA NDVI	60-68

PHEMA NDVM	60-88
PHEMA NDVQ	60-88
PHEMA NDVTG	60-88
PHEMA NDVU	60-88
PHEMA PIHW	20-60
PHEMA PI2H	13-48
PHEMA PI2HT	13-48
PHEMA PI3B	184-231
PHEMA PI3H4	184-231
PHEMA PI3HA	184-231
PHEMA PI3HT	184-231
PHEMA PI3HU	184-231
PHEMA PI3HV	184-231
PHEMA PI3HW	184-231
PHEMA PI3HX	184-231
PHEMA PI4HA	245-280
PHEMA RACM	265-283
PHEMA RINDL	282-313
PHEMA SENDG	16-64
PHEMA SENDF	16-64
PHEMA SENDH	16-64
PHEMA SENDJ	16-64
PHEMA SENDZ	23-54
PHEMA SV41	65-84
PHEMA SV6	7-35
PHEMA SV6CM	7-41
PHEMA SV6CP	7-41
PHEMA SV6LN	7-35
PHEMA VACC	268-284
PHEMA VACCI	259-284
PHEMA VACCT	268-284
PHEMA VACCV	268-284
PHEMA BEV	16-51
PYENV DHV1	287-335
PYENV MCV1	203-238
PYENV MCV2	203-238
PYENV VACCC	208-241
PYENV VACCI	208-241
PYENV VACCP	208-241
PYENV VACCY	208-241
PYF03 VACCC	2-40
PYF03 VACCV	2-40
PYFP1 FOWPV	297-330
PYFP4 FOWPV	237-267
PYFP7 CAPK	69-118
PYFR3 VACCC	28-61
PYFUS VACCV	28-61

PVG01 HSV1	917-946
PVG02 HSV/B	163-188
PVG02_VACC	92-120
PVG02_VARV	92-120
PVG03 HSV1	108-138
PVG03_HSV1	64-83
PVG03_VACC	69-139
PVG08 VARV	98-139
PVG07_VACC	113-145
PVG07_VARV	113-145
PVG09_VACC	303-338
PVG09_VACC	286-301
PVG09_VARV	303-338
PVG11 HSV1	160-183
PVG12 HSV1	206-243
PVG12_HSV/A	68-106
PVG13 HSV1	264-282
PVG13_SPV1R	303-337
PVG22 HSV1	300-337
PVG23 HSV1	70-108
PVG26 HSV1	84-125
PVG27 HSV/A	38-74
PVG28 HSV1	49-1521
PVG29 HSV/A	7-40
PVG2R AMEPV	180-217
PVG2 SPV4	208-244
PVG35 HSV1	16-46
PVG36 HSV/A	180-228
PVG36 HSV1	161-185
PVG39 HSV1	543-577
PVG40 HSV/A	187-216
PVG41 HSV1	11-46
PVG42 HSV1	91-126
PVG43 HSV1	109-140
PVG46 HSV1	688-825
PVG48 HSV/A	328-357
PVG50 HSV/A	113-141
PVG51 HSV1	28-64
PVG52 HSV1	66-134
PVG55 HSV1	100-129
PVG66 HSV1	631-667
PVG68 HSV1	342-376
PVG59 HSV/A	25-90
PVG69 HSV1	82-118
PVG61 HSV1	78-108
PVG64 HSV1	65-89
PVG65 HSV1	601-838
PVG67 HSV1	160-188
PVG68 SPV1R	60-89

PV071 HSV8A	128-168		
PV072 HSV11	446-478	720-781	1169-1189
PV073 HSV11	283-291	387-422	
PV076 HSV11	187-221		
PV07 8PV1R	18-48		
PV08F1 HSV11	1716-1747	1856-1881	2108-2146
PV0H3 HCMVA	80-116	187-188	3801-3833
PV0L2 CVBF	1256-1284		
PV0L2 CVBL0	881-981	1259-1294	
PV0L2 CVBLY		1268-1294	
PV0L2 CVBM		1269-1294	
PV0L2 CVBQ		1269-1294	
PV0L2 CVBV		1269-1294	
PV0L2 CVH22	1083-1088		
PV0L2 CVM4	1267-1304		
PV0L2 CVM45	1216-1252		
PV0L2 CVMJH	1126-1183		
PV0L2 CVPFB	632-986	720-784	1328-1363
PV0L2 CVPFU	630-983	734-762	1328-1381
PV0L2 CVPB	612-640	1104-1138	
PV0L2 CVPAM	408-441	1104-1139	
PV0L2 FPPV	636-988	738-787	1331-1366
PV0L2 IBV	163-188		
PV0LB HCMVA	116-147	708-743	
PV0LB HCMVIT	118-147	707-744	
PV0LB HAYEVU	72-110		
PV0LB HSVB1	264-288		
PV0LB HSVB2	264-288	745-774	
PV0LB HSVBC	263-287		
PV0LB ILTV6	442-472		
PV0LB ILTV9	482-482		
PV0LB ILTVT	462-482		
PV0LB MCMVB	136-163	738-776	
PV0LC HBV11	467-500		
PV0LC HSVIK	467-500		
PV0LC HSV2	435-465		
PV0LC HSV23	439-486		
PV0LC HAYBC	476-507		
PV0LC V2D	351-388	613-646	
PV0LC V2B	361-388	613-648	
PV0LD HAYEA	340-370		
PV0LD HSVB6	41-70	388-420	
PV0LD HSVBK	41-70	388-420	
PV0LE HSVE4	85-125		
PV0LE HSVEB	63-100	388-420	
PV0LE HSVEL	63-100	382-422	
PV0LE PAVRI	332-389		

PVGLF BRAVA	285-301	482-511
PVGLF BRBYC	484-513	
PVGLF BRBYR	484-513	
PVGLF CDVO	662-696	
PVGLF HRSV1	484-513	
PVGLF HRSVA	484-513	
PVGLF HRSVL	484-513	
PVGLF HRBYR	484-513	
PVGLF MEASE	224-256	451-484
PVGLF MEASI	227-269	454-497
PVGLF MEASY	224-266	451-494
PVGLF MUMPR	449-474	
PVGLF MUMPS	448-474	
PVGLF NDVI	132-166	448-474
PVGLF PHODY	631-666	
PVGLF P11HC	468-494	
PVGLF P13B	483-491	
PVGLF P13H4	463-491	
PVGLF RINDK	220-262	447-480
PVGLF RINDL	220-252	447-490
PVGLF BEND6	480-488	
PVGLF SENDF	480-488	
PVGLF SENDH	480-488	
PVGLF SENDJ	480-488	
PVGLF SENDZ	480-488	
PVGLF SVE	449-474	
PVGLF TATV	462-481	
PVGLG HAVEB	327-394	
PVGLG STNV	624-683	
PVGLQ VAVIG	450-488	
PVGLQ VBVJO	457-492	
PVGLQ VSVO	450-488	
PVGLQ VSVB	450-488	
PVGLH HCMVA	691-719	
PVGLH HCAYT	690-719	
PVGLH HAVEO	640-677	
PVGLH HAVEA	814-850	
PVGLH HAVEB	802-843	
PVGLI HCMVA	168-184	
PVGLM BUN92	197-227	438-468
PVGLM BUN17	180-220	
PVGLM BUN8H	180-220	344-381
PVGLM BUN9W	183-228	434-472
PVGLM DUGBY	244-273	687-722
PVGLM HANTB	610-641	1081-1119
PVGLM HANTH	186-222	612-643
		1082-1120

PVGLM_HANTL	188-222	612-643	1083-1121	
PVGLM_HANTV	188-222	612-643	1083-1121	
PVGLM_PHV	616-649	1088-1121		
PVGLM_PTV	949-982	1276-1308		
PVGLM_PUUMH	620-663	1092-1128		
PVGLM_PUUMS	620-663	1092-1126		
PVGLM_RVFV	620-653	630-893		
PVGLM_RVFVZ	620-653	630-853	1166-1186	
PVGLM_SEOUR	605-641	1082-1120		
PVGLM_SEOUS	610-641	1081-1119		
PVGLM_UUK	431-468	866-896		
PVGLP_BEV	1491-1628			
PVGLY_JUNIN	12-46			
PVGLY_LASQA	237-268			
PVGLY_LASBQ	238-366			
PVGLY_PIARV	12-60			
PVGLY_TACV	12-60	89-124		
PVGLY_TACV6	12-60	89-124		
PVGLY_TACV7	12-60	89-124		
PVGLY_TACVT	12-60	89-124		
PVGNB_CPNV	1627-1666			
PVGNN_8PMV	137-187	280-327	837-898	
PVGNN_CPMV	208-242	751-771		
PVGNN_CPSMV	50-86	478-516		
PVGNN_RCMV	789-799			
PVGQ2_EBV	7B-111			
PVGQ3_EBV	7B-111			
PVM1 REOVO	280-318	324-381		
PVM1 REOVL	280-318			
PVM21 REOVD	168-188			
PVM22 REOVD	168-188			
PVM2 REOJV	168-188			
PVM2 REOVL	168-188			
PVM3 REOVO	333-384			
PVMAT_SVE	208-342			
PVMAT_TRTV	122-160			
PVME1_CVBM	04-02			
PVME1_CVHOC	64-102			
PVME1_CVMA6	65-103			
PVME1_CVLMH	65-03			
PVME1_CVTE	64-102			
PVME1_EBV	178-213			
PVMP_CERV	03-128			
PVMP_SOCMV	68-88	273-303		
PVNISA_HPDBB	201-238	268-302		
PVNISA_HPDBC	194-227	268-301		
PVNISA_HPBDU	157-190	231-284		

PVMSA_HPBW	164-227	269-302
PVMSA_HPBGB	208-243	271-307
PVMSA_HPBHE	168-195	236-268
PVMSA_HPBVO	70-98	
PVMSA_HPBV2	244-272	
PVMSA_HPBV4	244-272	
PVMSA_HPBV6	244-272	
PVMSA_HPBV4	233-261	
PVMSA_HPBVD	70-98	
PVMSA_HPBVI	233-261	
PVMSA_HPBVJ	233-261	
PVMSA_HPBVL	233-261	
PVMSA_HPBVN	70-98	
PVMSA_HPBVO	233-261	
PVMSA_HPBVP	244-272	
PVMSA_HPBVR	244-272	
PVMSA_HPBV9	70-98	
PVMSA_HPBVW	233-261	
PVMSA_HPBVY	233-261	
PVMSA_HPBVZ	233-261	
PVMSA_WHV1	207-241	268-305
PVMSA_WHV5B	212-246	274-310
PVMSA_WHV7	212-246	274-310
PVMSA_WHVB	212-246	274-310
PVMSA_WHVB1	212-246	274-310
PVMSA_WHWB	125-161	
PVMT2_H211	10-44	
PVMTB_MYYVL	5-34	141-170
PVMTB_MYYVL	246-282	

5.3. SYNTHESIS OF PEPTIDES

The peptides of the invention may be synthesized or prepared by techniques well known in the art. See, for example, Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman and Co., NY,

5 which is incorporated herein by reference in its entirety. Short peptides, for example, can be synthesized on a solid support or in solution. Longer peptides may be made using recombinant DNA techniques.

10 Here, the nucleotide sequences encoding the peptides of the invention may be synthesized, and/or cloned, and expressed according to techniques well known to those of ordinary skill in the art. See, for example, Sambrook, *et al.*, 1989, Molecular Cloning, A

15 Laboratory Manual, Vols. 1-3, Cold Spring Harbor Press, NY.

The peptides of the invention may alternatively be synthesized such that one or more of the bonds which link the amino acid residues of the peptides are non-peptide bonds. These alternative non-peptide

20 bonds may be formed by utilizing reactions well known to those in the art, and may include, but are not limited to imino, ester, hydrazide, semicarbazide, and azo bonds, to name but a few. In yet another embodiment of the invention, peptides comprising the

25 sequences described above may be synthesized with additional chemical groups present at their amino and/or carboxy termini, such that, for example, the stability, bioavailability, and/or inhibitory activity of the peptides is enhanced. For example, hydrophobic

30 groups such as carbobenzoyl, dansyl, or t-butyoxy carbonyl groups, may be added to the peptides' amino termini. Likewise, an acetyl group or a 9-

35 fluorenylmethoxy-carbonyl group may be placed at the peptides' amino termini. (See "X" in Tables I to IV, above.) Additionally, the hydrophobic group, t-

butyloxycarbonyl, or an amido group may be added to the peptides' carboxy termini. (See "Z" in Tables I to IV, above.) Further, the peptides of the invention may be synthesized such that their steric configuration is altered. For example, the D-isomer of one or more of the amino acid residues of the peptide may be used, rather than the usual L-isomer. Still further, at least one of the amino acid residues of the peptides of the invention may be substituted by one of the well known non-naturally occurring amino acid residues. Alterations such as these may serve to increase the stability, bioavailability and/or inhibitory action of the peptides of the invention.

Any of the peptides described above may, additionally, have a non-peptide macromolecular carrier group covalently attached to their amino and/or carboxy termini. Such macromolecular carrier groups may include, for example, lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates. "X", in Tables I to IV, above, may therefore additionally represent any of the above macromolecular carrier groups covalently attached to the amino terminus of a peptide. Likewise, "Z", in Tables I to IV, may additionally represent any of the macromolecular carrier groups described above.

25

5.4. ASSAYS FOR ANTIVIRAL ACTIVITY

The antiviral activity exhibited by the peptides of the invention may be measured, for example, by easily performed in vitro assays, such as those described below, which can test the peptides' ability to inhibit syncytia formation, or their ability to inhibit infection by cell-free virus. Using these assays, such parameters as the relative antiviral activity of the peptides, exhibit against a given strain of virus and/or the strain specific inhibitory

activity of the peptide can be determined. A cell fusion assay may be utilized to test the peptides' ability to inhibit HIV-induced syncytia formation in vitro. Such an assay may comprise culturing uninfected CD-4⁺ cells (such as Molt or CEM cells, for example) in the presence of chronically HIV-infected cells and a peptide to be assayed. For each peptide, a range of peptide concentrations may be tested. This range should include a control culture wherein no peptide has been added. Standard conditions for culturing, well known to those of ordinary skill in the art, are used. After incubation for an appropriate period (24 hours at 37°C, for example) the culture is examined microscopically for the presence of multinucleated giant cells, which are indicative of cell fusion and syncytia formation.

A reverse transcriptase (RT) assay may be utilized to test the peptides' ability to inhibit infection of CD-4⁺ cells by cell-free HIV. Such an assay may comprise culturing an appropriate concentration (i.e., TCID₅₀) of virus and CD-4⁺ cells in the presence of the peptide to be tested. Culture conditions well known to those in the art are used. As above, a range of peptide concentrations may be used, in addition to a control culture wherein no peptide has been added. After incubation for an appropriate period (e.g., 7 days) of culturing, a cell-free supernatant is prepared, using standard procedures, and tested for the present of RT activity as a measure of successful infection. The RT activity may be tested using standard techniques such as those described by, for example, Goff et al. (Goff, S. et al., 1981, J. Virol. 38:239-248) and/or Willey et al. (Willey, R. et al., 1988, J. Virol. 62:139-147). These references are incorporated herein by reference in their entirety.

Standard methods which are well-known to those of skill in the art may be utilized for assaying non-retroviral activity. See, for example, Pringle et al. (Pringle, C.R. et al., 1985, J. Medical Virology 17:377-386) for a discussion of respiratory syncytial virus and parainfluenza virus activity assay techniques. Further, see, for example, "Zinsser Microbiology", 1988, Joklik, W.K. et al., eds., Appleton & Lange, Norwalk, CT, 19th ed., for a general review of such techniques. These references are incorporated by reference herein in its entirety.

5.5. USES OF THE PEPTIDES OF THE INVENTION

The DP-178 (SEQ ID:1) peptides of the invention, and DP-178 fragments, analogs, and homologs, exhibit potent antiviral activity. The DP-107-like and DP-178-like peptides of the invention preferably exhibit antiviral activity. As such, the peptides may be used as inhibitors of human and non-human viral and retroviral, especially HIV, transmission to uninfected cells.

The human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to all strains of HIV-1 and HIV-2 and the human T-lymphocyte viruses (HTLV-I and II). The non-human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to bovine leukosis virus, feline sarcoma and leukemia viruses, simian immunodeficiency, sarcoma and leukemia viruses, and sheep progressive pneumonia viruses.

Non retroviral viruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to human respiratory syncytial virus, canine distemper virus, newcastle disease virus, human parainfluenza virus, and influenza

viruses. Further, any virus or retrovirus containing peptides listed in Tables V through X above, may be inhibited by the peptides of the invention.

As discussed more fully, below, in Section 5.5.1 and in the Example presented, below, in Section 8, DP-
5 107 and DP-178, and DP-107-like and DP-178-like peptides form non-covalent protein-protein interactions which are required for normal activity of the virus. Thus, the peptides of the invention may also be utilized as components in assays for the
10 identification of compounds that interfere with such protein-protein interactions and may, therefore, act as antiviral agents. These assays are discussed, below, in Section 5.5.1.

15 5.5.1. ANTIVIRAL COMPOUND SCREENING SCREENING
ASSAYS FOR COMPOUNDS THAT INTERACT WITH
THE PKD1 GENE PRODUCT

As demonstrated in the Example presented in Section 8, below, DP-107 and DP-178 portions of the TM protein gp41 form non-covalent protein-protein interactions. As also demonstrated, the maintenance of such interactions is necessary for normal viral infectivity. Thus, compounds which bind DP-107, bind DP-178, and/or act to disrupt normal DP-107/DP-178
20 25 protein-protein interactions may act as potent antiviral agents. Described below are assays for the identification of such compounds. Note that, while, for ease and clarity of discussion, DP-107 and DP-178 peptides will be used as components of the assays described, but it is to be understood that any of the DP-107-like or DP-178-like peptides described, above,
30 35 in Sections 5.1 and 5.2 may also be utilized as part of these screens for antiviral compounds.

Compounds which may be tested for an ability to bind DP-107, DP-178, and/or disrupt DP-107/DP-178 interactions, and which therefore, potentially

represent antiviral compounds, include, but are not limited to, peptides made of D- and/or L-configuration amino acids (in, for example, the form of random peptide libraries; see Lam, K.S. *et al.*, 1991, *Nature* 354:82-84), phosphopeptides (in, for example, the form of random or partially degenerate, directed phosphopeptide libraries; see, for example, Songyang, Z. *et al.*, 1993, *Cell* 72:767-778), antibodies, and small organic or inorganic molecules. Synthetic compounds, natural products, and other sources of potentially effective materials may be screened in a variety of ways, as described in this Section. The compounds, antibodies, or other molecules identified may be tested for an ability to inhibit viral activity, utilizing, for example, viral assays such as those described, above, in Section 5.4.

Among the peptides which may be tested are soluble peptides comprising DP-107 and/or DP-178 domains, and peptides comprising DP-107 and/or DP-178 domains having one or more mutations within one or both of the domains, such as the M41-P peptide described, below, in the Example presented in Section 8, which contains a isoleucine to proline mutation within the DP-178 sequence.

In one embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

- (a) exposing at least one compound to a peptide comprising a DP-107 peptide for a time sufficient to allow binding of the compound to the DP-107 peptide;
- (b) removing non-bound compounds; and
- (c) determining the presence of the compound bound to the DP-107 peptide, thereby identifying an agent to be tested for antiviral ability.

In a second embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

(a) exposing at least one compound to a peptide comprising a DP-178 peptide for a time sufficient to allow binding of the compound to the DP-178 peptide;

(b) removing non-bound compounds; and
(c) determining the presence of the

compound bound to the DP-178 peptide,

thereby identifying an agent to be tested for antiviral ability.

One method utilizing these types of approaches that may be pursued in the isolation of such DP-107-binding or DP-178-binding compounds is an assay which would include the attachment of either the DP-107 or the DP-178 peptide to a solid matrix, such as, for example, agarose or plastic beads, microtiter plate wells, petri dishes, or membranes composed of, for example, nylon or nitrocellulose. In such an assay system, either the DP-107 or DP-178 protein may be anchored onto a solid surface, and the compound, or test substance, which is not anchored, is labeled, either directly or indirectly. In practice, microtiter plates are conveniently utilized. The anchored component may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying.

Alternatively, an immobilized antibody, preferably a monoclonal antibody, specific for the protein may be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

In order to conduct the assay, the labeled compound is added to the coated surface containing the anchored DP-107 or DP-178 peptide. After the reaction

is complete, unreacted components are removed (e.g., by washing) under conditions such that any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways.

- 5 Where the compound is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the labeled component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using
10 a labeled antibody specific for the compound (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody).

Alternatively, such an assay can be conducted in a liquid phase, the reaction products separated from
15 unreacted components, and complexes detected; e.g., using an immobilized antibody specific for DP-107 or DP-178, whichever is appropriate for the given assay, or an antibody specific for the compound, i.e., the test substance, in order to anchor any complexes
20 formed in solution, and a labeled antibody specific for the other member of the complex to detect anchored complexes.

By utilizing procedures such as this, large numbers of types of molecules may be simultaneously
25 screened for DP-107 or DP-178-binding capability, and thus potential antiviral activity.

Further, compounds may be screened for an ability to inhibit the formation of or, alternatively, disrupt DP-107/DP-178 complexes. Such compounds may then be
30 tested for antiviral capability. For ease of description, DP-107 and DP-178 will be referred to as "binding partners." Compounds that disrupt such interactions may exhibit antiviral activity. Such compounds may include, but are not limited to

molecules such as antibodies, peptides, and the like described above.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the DP-107 and DP-178 peptides involves preparing a reaction mixture containing peptides under conditions and for a time sufficient to allow the two peptides to interact and bind, thus forming a complex. In order to test a compound for disruptive activity, the reaction is conducted in the presence and absence of the test compound, i.e., the test compound may be initially included in the reaction mixture, or added at a time subsequent to the addition of one of the binding partners; controls are incubated without the test compound or with a placebo. The formation of any complexes between the binding partners is then detected. The formation of a complex in the control reaction, but not in the reaction mixture containing the test compound indicates that the compound interferes with the interaction of the DP-107 and DP-178 peptides.

The assay for compounds that interfere with the interaction of the binding partners can be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring one of the binding partners onto a solid phase and detecting complexes anchored on the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the binding partners, e.g., by competition, can be identified by conducting the reaction in the presence of the test substance; i.e., by adding the test

substance to the reaction mixture prior to or simultaneously with the binding partners. On the other hand, test compounds that disrupt preformed complexes, e.g., compounds with higher binding constants that displace one of the binding partners from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are described briefly below.

In a heterogeneous assay system, one binding partner, e.g., either the DP-107 or DP-178 peptide, is anchored onto a solid surface, and its binding partner, which is not anchored, is labeled, either directly or indirectly. In practice, microtiter plates are conveniently utilized. The anchored species may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying. Alternatively, an immobilized antibody specific for the protein may be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

In order to conduct the assay, the binding partner of the immobilized species is added to the coated surface with or without the test compound. After the reaction is complete, unreacted components are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the binding partner was pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the binding partner is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for

the binding partner (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which inhibit complex formation or which disrupt preformed complexes can be detected.

Alternatively, the reaction can be conducted in a liquid phase in the presence or absence of the test compound, the reaction products separated from unreacted components, and complexes detected; e.g., using an immobilized antibody specific for one binding partner to anchor any complexes formed in solution, and a labeled antibody specific for the other binding partner to detect anchored complexes. Again, depending upon the order of addition of reactants to the liquid phase, test compounds which inhibit complex or which disrupt preformed complexes can be identified.

In an alternate embodiment of the invention, a homogeneous assay can be used. In this approach, a preformed complex of the DP-107 and DP-178 peptides is prepared in which one of the binding partners is labeled, but the signal generated by the label is quenched due to complex formation (see, e.g., U.S. Patent No. 4,109,496 by Rubenstein which utilizes this approach for immunoassays). The addition of a test substance that competes with and displaces one of the binding partners from the preformed complex will result in the generation of a signal above background. In this way, test substances which disrupt DP-107/DP-178 protein-protein interaction can be identified.

5.5 PHARMACEUTICAL FORMULATIONS, DOSAGES AND MODES OF ADMINISTRATION

With respect to HIV, the peptides of the invention may be used as a therapeutic in the

treatment of AIDS. The peptides of the invention may be administered using techniques well known to those in the art. Preferably, agents are formulated and administered systemically. Techniques for formulation and administration may be found in "Remington's Pharmaceutical Sciences", 18th ed., 1990, Mack Publishing Co., Easton, PA. Suitable routes may include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections, just to name a few. Most preferably, administration is intravenous. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiological saline buffer. For such transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

In addition, the peptides may be used as a prophylactic measure in previously uninfected individuals after acute exposure to an HIV virus.

Examples of such prophylactic use of the peptides may include, but are not limited to, prevention of virus transmission from mother to infant and other settings where the likelihood of HIV transmission exists, such as, for example, accidents in health care settings wherein workers are exposed to HIV-containing blood products. The peptides of the invention in such cases may serve the role of a prophylactic vaccine, wherein the host raises antibodies against the peptides of the invention, which then serve to neutralize HIV viruses by, for example, inhibiting further HIV infection.

Administration of the peptides of the invention as a prophylactic vaccine, therefore, would comprise administering to a host a concentration of peptides effective in raising an immune response which is sufficient to neutralize HIV, by, for example,

5 inhibiting HIV ability to infect cells. The exact concentration will depend upon the specific peptide to be administered, but may be determined by using standard techniques for assaying the development of an immune response which are well known to those of
10 ordinary skill in the art. The peptides to be used as vaccines are usually administered intramuscularly.

The peptides may be formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants may include, but are not
15 limited to mineral gels such as aluminum hydroxide; surface active substances such as lysolecithin, pluronic polyols, polyanions; other peptides; oil emulsions; and potentially useful human adjuvants such as BCG and *Corynebacterium parvum*. Many methods may
20 be used to introduce the vaccine formulations described here. These methods include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes.

25 Alternatively, an effective concentration of polyclonal or monoclonal antibodies raised against the peptides of the invention may be administered to a host so that no uninfected cells become infected by HIV. The exact concentration of such antibodies will
30 vary according to each specific antibody preparation, but may be determined using standard techniques well known to those of ordinary skill in the art. Administration of the antibodies may be accomplished using a variety of techniques, including, but not
35 limited to those described in this section.

Effective dosages of the peptides of the invention to be administered may be determined through procedures well known to those in the art which address such parameters as biological half-life, bioavailability, and toxicity. Given the data 5 presented below in Section 6, DP-178, for example, may prove efficacious in vivo at doses required achieve circulating levels of 10ng per ml of peptide.

A therapeutically effective dose refers to that amount of the compound sufficient to result in 10 amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 15 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds 20 which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of 25 circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the 30 therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 (i.e., the concentration of the test compound which 35 achieves a half-maximal disruption of the PTK/adaptor

prot in complex, or a half-maximal inhibition of the cellular level and/or activity of a complex component) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for 5 example, by high performance liquid chromatography (HPLC).

The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g. Fingl 10 et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p1).

It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity, or to organ 15 dysfunctions. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administrated dose in the management of the oncogenic disorder of interest 20 will vary with the severity of the condition to be treated and to the route of administration. The dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that 25 discussed above may be used in veterinary medicine.

As demonstrated in the Example presented below in Section 6, the antiviral activity of the peptides of the invention may show a pronounced type and subtype specificity, i.e., specific peptides may be effective 30 in inhibiting the activity of only specific viruses. This feature of the invention presents many advantages. One such advantage, for example, lies in the field of diagnostics, wherein one can use the 35 antiviral specificity of the peptide of the invention to ascertain the identity of a viral isolate. With

respect to HIV, one may easily determine whether a viral isolate consists of an HIV-1 or HIV-2 strain. For example, uninfected CD-4⁺ cells may be co-infected with an isolate which has been identified as containing HIV the DP-178 (SEQ ID:1) peptide, after which the retroviral activity of cell supernatants may be assayed, using, for example, the techniques described above in Section 5.2. Those isolates whose retroviral activity is completely or nearly completely inhibited contain HIV-1. Those isolates whose viral activity is unchanged or only reduced by a small amount, may be considered to not contain HIV-1. Such an isolate may then be treated with one or more of the other DP-178 peptides of the invention, and subsequently be tested for its viral activity in order to determine the identify of the viral isolate.

Use of pharmaceutically acceptable carriers to formulate the compounds herein disclosed for the practice of the invention into dosages suitable for systemic administration is within the scope of the invention. With proper choice of carrier and suitable manufacturing practice, the compositions of the present invention, in particular, those formulated as solutions, may be administered parenterally, such as by intravenous injection. The compounds can be formulated readily using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral administration. Such carriers enable the compounds of the invention to be formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. Determination

of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable 5 pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, 10 dragees, capsules, or solutions.

The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, e.g., by means of conventional mixing, 15 dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, 20 suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. 25 Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the 30 solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical preparations for oral use can be obtained by combining the active compounds with solid excipient, optionally grinding a resulting mixture, 35 and processing the mixture of granules, after adding

suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch,
5 potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone,
10 agar, or alginic acid or a salt thereof such as sodium alginate.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc,
15 polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize
20 different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The
25 push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

6. EXAMPLE: DP-178 (SEQ ID:1) IS A POTENT
INHIBITOR OF HIV-1 INFECTION

In this example, DP-178 (SEQ ID:1) is shown to be a potent inhibitor of HIV-1 mediated CD-4⁺ cell-cell fusion and infection by cell free virus. In the 5 fusion assay, this peptide completely blocks virus induced syncytia formation at concentrations of from 1-10 ng/ml. In the infectivity assay the inhibitory concentration is somewhat higher, blocking infection at 90ng/ml. It is further shown that DP-178 (SEQ 10 ID:1) shows that the antiviral activity of DP-178 (SEQ ID:1) is highly specific for HIV-1. Additionally, a synthetic peptide, DP-185 (SEQ ID:3), representing a HIV-1-derived DP-178 homolog is also found to block HIV-1-mediated syncytia formation.

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6.1. MATERIALS AND METHODS

6.1.1. PEPTIDE SYNTHESIS

Peptides were synthesized using Fast Moc 20 chemistry on an Applied Biosystems Model 431A peptide synthesizer. Amidated peptides were prepared using Rink resin (Advanced Chemtech) while peptides containing free carboxy termini were synthesized on Wang (p-alkoxy-benzyl-alcohol) resin (Bachem). First 25 residues were double coupled to the appropriate resin and subsequent residues were single coupled. Each coupling step was followed by acetic anhydride capping. Peptides were cleaved from the resin by treatment with trifluoracetic acid (TFA) (10ml), H₂O 30 (0.5ml), thioanisole (0.5ml), ethanedithiol (0.25ml), and crystalline phenol (0.75g). Purification was carried out by reverse phase HPLC. Approximately 50mg samples of crude peptide were chromatographed on a Waters Delta Pak C18 column (19mm x 30cm, 15 μ 35 spherical) with a linear gradient; H₂O/acetonitrile

0.1% TFA. Lyophilized peptides were stored desiccated and peptide solutions were made in water at about 1mg/ml. Electrospray mass spectr metry yielded the following results: DP-178 (SEQ ID:1):4491.87 (calculated 4491.94); DP-180 (SEQ ID:2):4491.45 (calculated 4491.94); DP-185 (SEQ ID:3):not done (calculated 4546.97).

6.1.2. VIRUS

The HIV-1_{LAI} virus was obtained from R. Gallo (Popovic, M. et al., 1984, Science 224:497-508) and propagated in CEM cells cultured in RPMI 1640 containing 10% fetal calf serum. Supernatant from the infected CEM cells was passed through a 0.2μm filter and the infectious titer estimated in a microinfectivity assay using the AA5 cell line to support virus replication. For this purpose, 25μl of serial diluted virus was added to 75μl AA5 cells at a concentration of 2×10^5 /ml in a 96-well microtitre plate. Each virus dilution was tested in triplicate. Cells were cultured for eight days by addition of fresh medium every other day. On day 8 post infection, supernatant samples were tested for virus replication as evidenced by reverse transcriptase activity released to the supernatant. The TCID₅₀ was calculated according to the Reed and Muench formula (Reed, L.J. et al., 1938, Am. J. Hyg. 27:493-497). The titer of the HIV-1_{LAI} and HIV-1_{MN} stocks used for these studies, as measured on the AA5 cell line, was approximately 1.4×10^6 and 3.8×10^4 TCID₅₀/ml, respectively.

6.1.3. CELL FUSION ASSAY

Approximately 7×10^4 Molt cells were incubated with 1×10^4 CEM cells chronically infected with the HIV-1_{LAI} virus in 96-well plates (one-half area cluster plates; Costar, Cambridge, MA) in a final volume of

100 μ l culture medium as previously described (Matthews, T.J. et al., 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5428). Peptide inhibitors were added in a volume of 10 μ l and the cell mixtures were incubated for 24 hr. at 37°C. At that time, multinucleated giant cells were estimated by microscopic examination at a 40x magnification which allowed visualization of the entire well in a single field.

6.1.4. CELL FREE VIRUS INFECTION ASSAY

Synthetic peptides were incubated at 37°C with either 247 TCID₅₀ (for experiment depicted in FIG. 2), or 62 TCID₅₀ (for experiment depicted in FIG. 3) units of HIV-1_{LA1} virus or 25 TCID₅₀ units of HIV-2_{NH2} and CEM CD4⁺ cells at peptide concentrations of 0, 0.04, 0.4, 4.0, and 40 μ g/ml for 7 days. The resulting reverse transcriptase (RT) activity in counts per minute was determined using the assay described, below, in Section 6.1.5. See, Reed, L.J. et al., 1938, Am. J. Hyg. 27: 493-497 for an explanation of TCID₅₀ calculations.

6.1.5. REVERSE TRANSCRIPTASE ASSAY

The micro-reverse transcriptase (RT) assay was adapted from Goff et al. (Goff, S. et al., 1981, J. Virol. 38:239-248) and Willey et al. (Willey, R. et al., 1988, J. Virol. 62:139-147). Supernatants from virus/cell cultures are adjusted to 1% Triton-X100. A 10 μ l sample of supernatant was added to 50 μ l of RT cocktail in a 96-well U-bottom microtitre plate and the samples incubated at 37°C for 90 min. The RT cocktail contained 75mM KCl, 2mM dithiothreitol, 5mM MgCl₂, 5 μ g/ml poly A (Pharmacia, cat. No. 27-4110-01), 0.25 units/ml oligo dT (Pharmacia, cat. No. 27-7858-01), 0.05% NP40, 50mM Tris-HCl, pH 7.8, 0.5 μ M non-

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radioactive dTTP, and $10\mu\text{Ci}/\text{ml}$ ^{32}P -dTTP (Amersham, cat. No. PB.10167).

After the incubation period, $40\mu\text{l}$ of reaction mixture was applied to a Schleicher and Schuell (S+S) NA45 membrane (or DE81 paper) saturated in 2 x SSC buffer (0.3M NaCl and 0.003M sodium citrate) held in a S+S Minifold over one sheet of GB003 (S+S) filter paper, with partial vacuum applied. Each well of the minifold was washed four times with $200\mu\text{l}$ 2xSSC, under full vacuum. The membrane was removed from the

minifold and washed 2 more times in a pyrex dish with an excess of 2xSSC. Finally, the membrane was drained on absorbent paper, placed on Whatman #3 paper, covered with Saran wrap, and exposed to film overnight at -70°C .

15

6.2. RESULTS

6.2.1. PEPTIDE INHIBITION OF INFECTED CELL-INDUCED SYNCYTIA FORMATION

20 The initial screen for antiviral activity assayed peptides' ability to block syncytium formation induced by overnight co-cultivation of uninfected Molt4 cells with chronically HIV-1 infected CEM cells. The results of several such experiments are presented
25 herein. In the first of these experiments, serial DP-178 (SEQ ID:1) peptide concentrations between $10\mu\text{g}/\text{ml}$ and $12.5\text{ng}/\text{ml}$ were tested for blockade of the cell fusion process. For these experiments, CEM cells chronically infected with either HIV-1_{LA1}, HIV-1_{MN}, HIV-
30 1_{KP}, or HIV-1_{SP2} virus were cocultivated overnight with uninfected Molt 4 cells. The results (FIG. 4) show that DP-178 (SEQ ID:1) afforded complete protection against each of the HIV-1 isolates down to the lowest concentration of DP-178 (SEQ ID:1) used. For HIV_{LA1}
35 inhibition, the lowest concentration tested was

12.5ng/ml; for all other HIV-1 viruses, the lowest concentration of DP-178 (SEQ ID:1) used in this study was 100ng/ml. A second peptide, DP-180 (SEQ ID:2), containing the same amino acid residues as DP-178 (SEQ ID:1) but arranged in a random order exhibited no evidence of anti-fusogenic activity even at the high concentration of 40 μ g/ml (FIG. 4). These observations indicate that the inhibitory effect of DP-178 (SEQ ID:1) is primary sequence-specific and not related to non-specific peptide/protein interactions. The actual endpoint (*i.e.*, the lowest effective inhibitory concentration) of DP-178 inhibitory action is within the range of 1-10 ng/ml.

The next series of experiments involved the preparation and testing of a DP-178 (SEQ ID:1) homolog for its ability to inhibit HIV-1-induced syncytia formation. As shown in FIG. 1, the sequence of DP-185 (SEQ ID:3) is slightly different from DP-178 (SEQ ID:1) in that its primary sequence is taken from the HIV-1_{SP2} isolate and contains several amino acid differences relative to DP-178 (SEQ ID:1) near the N terminus. As shown in FIG. 4, DP-185 (SEQ ID:3), exhibits inhibitory activity even at 312.5ng/ml, the lowest concentration tested.

The next series of experiments involved a comparison of DP-178 (SEQ ID:1) HIV-1 and HIV-2 inhibitory activity. As shown in FIG. 5, DP-178 (SEQ ID:1) blocked HIV-1-mediated syncytia formation at peptide concentrations below 1ng/ml. DP-178 (SEQ ID:1) failed, however, to block HIV-2 mediated syncytia formation at concentrations as high as 10 μ g/ml. This striking 4 log selectivity of DP-178 (SEQ ID:1) as an inhibitor of HIV-1-mediated cell fusion demonstrates an unexpected HIV-1 specificity in the action of DP-178 (SEQ ID:1). DP-178 (SEQ ID:1) inhibition of HIV-1-mediated cell fusion, but the

peptide's inability to inhibit HIV-2 mediated cell fusion in the same cell type at the concentrations tested provides further evidence for the high degree of selectivity associated with the antiviral action of DP-178 (SEQ ID:1).

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6.2.2. PEPTIDE INHIBITION OF INFECTION BY CELL-FREE VIRUS

DP-178 (SEQ ID:1) was next tested for its ability to block CD-4⁺ CEM cell infection by cell free HIV-1 virus. The results, shown in FIG. 2, are from an experiment in which DP-178 (SEQ ID:1) was assayed for its ability to block infection of CEM cells by an HIV-1_{LAI} isolate. Included in the experiment were three control peptides, DP-116 (SEQ ID:9), DP-125 (SEQ ID:8), and DP-118 (SEQ ID:10). DP-116 (SEQ ID:9) represents a peptide previously shown to be inactive using this assay, and DP-125 (SEQ ID:8; Wild, C. *et al.*, 1992, Proc. Natl. Acad. Sci. USA 89:10,537) and DP-118 (SEQ ID:10) are peptides which have previously been shown to be active in this assay. Each concentration (0, 0.04, 0.4, 4, and 40 μ g/ml) of peptide was incubated with 247 TCID₅₀ units of HIV-1_{LAI} virus and CEM cells. After 7 days of culture, cell-free supernatant was tested for the presence of RT activity as a measure of successful infection. The results, shown in FIG. 2, demonstrate that DP-178 (SEQ ID:1) inhibited the de novo infection process mediated by the HIV-1 viral isolate at concentrations as low as 90ng/ml (IC50=90ng/ml). In contrast, the two positive control peptides, DP-125 (SEQ: ID:8) and DP-118 (SEQ ID:10), had over 60-fold higher IC50 concentrations of approximately 5 μ g/ml.

In a separate experiment, the HIV-1 and HIV-2 inhibitory action of DP-178 (SEQ ID:1) was tested with CEM cells and either HIV-1_{LAI} or HIV-2_{NMZ}. 62 TCID₅₀

HIV-1_{LAI} or 25 GCID₅₀ HIV-2_{NH2Z} were used in these experiments, and were incubated for 7 days. As may be seen in FIG. 3, DP-178 (SEQ ID:1) inhibited HIV-1 infection with an IC₅₀ of about 31ng/ml. In contrast, DP-178 (SEQ ID:1) exhibited a much higher IC₅₀ for HIV-2_{NH2Z}, thus making DP-178 (SEQ ID:1) two logs more potent as a HIV-1 inhibitor than a HIV-2 inhibitor. This finding is consistent with the results of the fusion inhibition assays described, above, in Section 6.2.1, and further supports a significant level of selectivity (*i.e.*, for HIV-1 over HIV-2).

7. EXAMPLE: THE HIV-1 INHIBITOR, DP-178 (SEQ ID:1) IS NON-CYTOXIC

In this Example, the 36 amino acid synthetic peptide inhibitor DP-178 (SEQ ID:1) is shown to be non-cytotoxic to cells in culture, even at the highest peptide concentrations (40 μ g/ml) tested.

7.1. MATERIALS AND METHODS

Cell proliferation and toxicity assay:
Approximately 3.8×10^5 CEM cells for each peptide concentration were incubated for 3 days at 37°C in T25 flasks. Peptides tested were DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9), as described in FIG. 1. The concentrations of each peptide used were 0, 2.5, 10, and 40 μ g/ml. Cell counts were taken at incubation times of 0, 24, 48, and 72 hours.

7.2. RESULTS

Whether the potent HIV-1 inhibitor DP-178 (SEQ ID:1) exhibited any cytotoxic effects was assessed by assaying the peptide's effects on the proliferation and viability of cells in culture. CEM cells were incubated in the presence of varying concentrations of DP-178 (SEQ ID:1), and DP-116 (SEQ ID:9), a peptide

previously shown to be ineffective as a HIV inhibitor (Wild, C. et al., 1992, Proc. Natl. Acad. Sci. USA 89:10,537-10,541). Additionally, cells were incubated in the absence of either peptide.

The results of the cytotoxicity study demonstrate that DP-178 (SEQ ID:1) exhibits no cytotoxic effects on cells in culture. As can be seen, below, in Table XI, even the proliferation and viability characteristics of cells cultured for 3 days in the presence of the highest concentration of DP-178 (SEQ ID:1) tested (40 μ g/ml) do not significantly differ from the DP-116 (SEQ ID:9) or the no-peptide controls. The cell proliferation data is also represented in graphic form in FIG. 6. As was demonstrated in the Working Example presented above in Section 6, DP-178 (SEQ ID:1) completely inhibits HIV-1 mediated syncytia formation at peptide concentrations between 1 and 10ng/ml, and completely inhibits cell-free viral infection at concentrations of at least 90ng/ml. Thus, this study demonstrates that even at peptide concentrations greater than 3 log higher than the HIV inhibitory dose, DP-178 (SEQ ID:1) exhibits no cytotoxic effects.

TABLE XI

25

	<u>Peptide</u>	<u>Concentration μg/ml</u>	% Viability at time (hours)			
			0	24	48	72
30	DP178 (SEQ ID:1)	40		98	97	95
		10		98	97	98
		2.5		98	93	96

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	DP116 (SEQ ID:9)	40	98	95	98	97
		10	98	95	93	98
		2.5	98	96	98	99
5						
	No Peptide	0	98	97	99	98

10 8. EXAMPLE: THE INTERACTION OF DP178 AND DP107

Soluble recombinant forms of gp41 used in the example described below provide evidence that the DP178 peptide associates with a distal site on gp41 whose interactive structure is influenced by the DP107 leucine zipper motif. A single mutation disrupting the coiled-coil structure of the leucine zipper domain transformed the soluble recombinant gp41 protein from an inactive to an active inhibitor of HIV-1 fusion. This transformation may result from liberation of the potent DP178 domain from a molecular clasp with the leucine zipper, DP107, determinant. The results also indicate that the anti-HIV activity of various gp41 derivatives (peptides and recombinant proteins) may be due to their ability to form complexes with viral gp41 and interfere with its fusogenic process.

20 8.1. MATERIALS AND METHODS

25 8.1.1. CONSTRUCTION OF FUSION PROTEINS
AND GP41 MUTANTS

30 Construction of fusion proteins and mutants shown in FIG. 7 was accomplished as follows: the DNA sequence corresponding to the extracellular domain of gp41 (540-686) was cloned into the Xmn I site of the expression vector pMal-p2 (New England Biolab) to give M41. The gp41 sequence was amplified from pgtat

(Malim et al., 1988, Nature 355: 181-183) by using polymerase chain r action (PCR) with upstream primer 5'-ATGACGCTGACGGTACAGGCC-3' (primer A) and downstream primer 5'-TGACTAAGCTTAATACCACAGCCAATTGTTAT-3' (primer B). M41-P was constructed by using the T7-Gen 5 in vitro mutagenesis kit from United States Biochemicals (USB) following the supplier's instructions. The mutagenic primer (5'-GGAGCTGCTGGGGCCCCAGAC-3') introduces an Ile to Pro mutation in M41 at position 578. M41Δ107 was made 10 using a deletion mutagenic primer 5'-CCAAATCCCCAGGAGCTGCTCGAGCTGCACTATACCAGAC-3' (primer C) following the USB T7-Gen mutagenesis protocol. M41Δ178 was made by cloning the DNA fragment corresponding to gp41 amino acids 540-642 into the Xmn 15 I site of pMal-p2. Primer A and 5'-ATAGCTTCTAGATTAATTGTTAATTCTCTGTCCC-3' (primer D) were used in the PCR with the template pgtat to generate the inserted DNA fragments. M41-P was used as the template with primer A and D in PCR to generate M41- 20 Δ178. All inserted sequences and mutated residues were checked by restriction enzyme analysis and confirmed by DNA sequencing.

25 8.1.2. PURIFICATION AND CHARACTERIZATION OF FUSION PROTEINS

The fusion proteins were purified according to the protocol described in the manufacturer's brochure of protein fusion and purification systems from New England Biolabs (NEB). Fusion proteins (10 ng) were 30 analyzed by electrophoresis on 8% SDS polyacrylamide gels. Western blotting analysis was performed as described by Sambrook et al, 1989, Molecular Cloning: A Laboratory Manual, 2d Ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, Ch. 18, 35 pp. 64-75. An HIV-1 positive serum diluted 1000-fold,

or a human Fab derived from repertoire cloning was used to react with the fusion proteins. The second antibody was HRP-conjugated goat antihuman Fab. An ECL Western blotting detection system (Amersham) was used to detect the bound antibody. A detailed protocol for this detection system was provided by the manufacturer. Rainbow molecular weight marker (Amersham) were used to estimate the size of fusion proteins.

10 8.1.3. CELL FUSION ASSAYS FOR ANTI-HIV ACTIVITY

Cell fusion assays were performed as previously described (Matthews et al., 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5481). CEM cells (7×10^4) were incubated with HIV-1_{MM} chronically infected CEM cells (10^4) in 96-well flat-bottomed half-area plates (Costar) in 100 μ l culture medium. Peptide and fusion proteins at various concentrations in 10 μ l culture medium were incubated with the cell mixtures at 37°C for 24 hours. Multinucleated syncytia were estimated with microscopic examination. Both M41 and M41-P did not show cytotoxicity at the concentrations tested and shown in FIG. 8.

Inhibition of HIV-1 induced cell-cell fusion activity was carried out in the presence of 10 nM DP178 and various concentrations of M41 Δ 178 or M41-P Δ 178 as indicated in FIG. 9. There was no observable syncytia in the presence of 10 nM DP178. No peptide or fusion protein was added in the control samples.

30 8.1.4. ELISA ANALYSIS OF DP178 BINDING TO THE LEUCINE ZIPPER MOTIF OF GP41

The amino acid sequence of DP178 used is:
YTSЛИHSLIEESQNQQEKNEQELLELDKWASLWNWF. For enzyme linked immunoassay (ELISA), M41 Δ 178 or M41-P Δ 178 (5 μ g/ml) in 0.1M NaHCO₃, pH 8.6, were coated on 96 wells

Linbro ELISA plates (Flow Lab, Inc.) overnight. Each well was washed three times with distilled water then blocked with 3% bovine serum albumin (BSA) for 2 hours. After blocking, peptides with 0.5% BSA in TBST (40 mM Tris-HCl pH7.5, 150 mM NaCl, 0.05% Tween 20) were added to the ELISA plates and incubated at room temperature for 1 hour. After washing three times with TBST, Fab-d was added at a concentration of 10 ng/ml with 0.5% BSA in TBST. The plates were washed three times with TBST after incubation at room temperature for 1 hour. Horse radish peroxidase (HRP) conjugated goat antihuman Fab antiserum at a 2000 fold dilution in TBST with 0.5% BSA was added to each well and incubated at room temperature for 45 minutes. The plates were then washed four times with TBST. The peroxidase substrate o-phenylene diamine (2.5 mg/ml) and 0.15% H₂O₂ were added to develop the color. The reaction was stopped with an equal volume of 4.5 N H₂SO₄ after incubation at room temperature for 10 minutes. The optical density of the stopped reaction mixture was measured with a micro plate reader (Molecular Design) at 490 nm. Results are shown in FIG. 10.

8.2. RESULTS

8.2.1. THE EXPRESSION AND CHARACTERIZATION OF THE ECTODOMAIN OF GP41

As a step toward understanding the roles of the two helical regions in gp41 structure and function, the ectodomain of gp41 was expressed as a maltose binding fusion protein (M41) (Fig. 7). The fusogenic peptide sequence at the N-terminal of gp41 was omitted from this recombinant protein and its derivatives to improve solubility. The maltose binding protein facilitated purification of the fusion proteins under relatively mild, non-denaturing conditions. Because

the M41 soluble r combinant gp41 was not glycosylated, lacked several regions of the transmembrane protein (*i.e.*, the fusion peptid , the membrane spanning, and the cytoplasmic domains), and was expressed in the absence of gp120, it was not expected to precisely reflect the structure of native gp41 on HIV-1 virions. Nevertheless, purified M41 folded in a manner that preserved certain discontinuous epitopes as evidenced by reactivity with human monoclonal antibodies, 98-6, 126-6, and 50-69, previously shown to bind conformational epitopes on native gp41 expressed in eukaryotic cells (Xu et al., 1991, J. Virol. 65: 4832-4838; Chen, 1994, J. Virol. 68:2002-2010). Thus, at least certain regions of native gp41 defined by these antibodies appear to be reproduced in the recombinant fusion protein M41. Furthermore, M41 reacted with a human recombinant Fab (Fab-d) that recognizes a conformational epitope on gp41 and binds HIV-1 virions as well as HIV-1 infected cells but not uninfected cells as analyzed by FACS. Deletion of either helix motif, *i.e.*, DP107 or DP178, of the M41 fusion protein eliminated reactivity with Fab-d. These results indicate that both helical regions, separated by 60 amino acids in the primary sequence, are required to maintain the Fab-d epitope.

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8.2.2. ANTI-HIV ACTIVITY OF THE RECOMBINANT ECTODOMAIN OF GP41

The wild type M41 fusion protein was tested for anti-HIV-1 activity. As explained, *supra*, synthetic peptides corresponding to the leucine zipper (DP107) and the C-terminal putative helix (DP178) show potent anti-HIV activity. Despite inclusion of both these regions, the recombinant M41 protein did not affect

35

HIV-1 induced membrane fusion at concentrations as high as 50 μ M (Table XII, below).

TABLE XII
**DISRUPTION OF THE LEUCINE ZIPPER OF
 GP41 FREES THE ANTI-HIV MOTIF**

		<u>DP107</u>	<u>DP178</u>	<u>M41</u>	<u>M41-P</u>	<u>M41-PΔ178</u>
5	Cell fusion (IC ₅₀)	1 μ M	1 nM	> 50 μ M	83 nM	> 50 μ M
10	Fab-D binding (k_D)	-	-	3.5x10 ⁹	2.5x10 ⁹	-
15	HIV infectiv- ity (IC ₅₀)	1 μ M	80 nM	> 16 μ M	66 nM	> 8 μ M

1 The affinity constants of Fab-d binding to the fusion proteins were determined using a protocol described by B. Friguet et al., 1985, J. Immunol. Method. 77:305-319.

20 - = No detectable binding of Fab-d to the fusion proteins.

25 *Antiviral Infectivity Assays.* 20 μ l of serially diluted virus stock was incubated for 60 minutes at ambient temperature with 20 μ l of the indicated concentration of purified recombinant fusion protein in RPMI 1640 containing 10% fetal bovine serum and antibiotics in a 96-well microtiter plate. 20 μ l of CEM4 cells at 6×10^3 cells/ml were added to each well, and cultures were incubated at 37°C in a humidified CO₂ incubator. Cells were cultured for 9 days by the addition of fresh medium every 2 to 30 days. On days 5, 7, and 9 postinfection, supernatant samples were assayed for reverse transcriptase (RT) activity, as described below, to monitor viral replication. The 50% tissue culture infectious dose (TCID₅₀) was calculated for each condition according to the formula of Reed & Muench, 1937, Am. J. Hyg. 27:493-497. RT activity was determined by a modification of the published methods of Goff et al., 1981, J. Virol. 38:239-248 and Willey et al., 1988, J. Virol. 62:139-147 as described in Chen et al., 1993, AIDS Res. Human Retroviruses 9:1079-1086.

30 Surprisingly, a single amino acid substitution, proline in place of isoleucine in the middle of the leucine zipper motif, yielded a fusion protein (M41-P)

which did exhibit antiviral activity (Table XII and Fig. 8). As seen in Table XII, M41-P blocked syncytia formation by 90% at approximately 85 nM and neutralized HIV-1_{MB} infection by 90% at approximately 70 nM concentrations. The anti-HIV-1 activity of M41-P appeared to be mediated by the C-terminal helical sequence since deletion of that region from M41-P yielded an inactive fusion protein, M41- Δ 178 (Table XII). That interpretation was reinforced by experiments demonstrating that a truncated fusion protein lacking the DP178 sequence, M41 Δ 178, abrogated the potent anti-fusion activity of the DP178 peptide in a concentration-dependent manner (FIG. 9). The same truncated fusion protein containing the proline mutation disrupting the leucine zipper, M41- Δ 178, was not active in similar competition experiments (FIG. 9). The results indicate that the DP178 peptide associates with a second site on gp41 whose interactive structure is dependent on a wild type leucine zipper sequence. A similar interaction may occur within the wild type fusion protein, M41, and act to form an intramolecular clasp which sequesters the DP178 region, making it unavailable for anti-viral activity.

A specific association between these two domains is also indicated by other human monoclonal Fab-d studies. For example, Fab-d failed to bind either the DP178 peptide or the fusion protein M41 Δ 178, but its epitope was reconstituted by simply mixing these two reagents together (FIG. 10). Again, the proline mutation in the leucine zipper domain of the fusion protein, M41- Δ 178, failed to reconstitute the epitope in similar mixing experiments.

9. EXAMPLE: METHOD FOR COMPUTER-ASSISTED
IDENTIFICATION OF DP-107-LIKE
AND DP-178-LIKE SEQUENCES

A number of known coiled-coil sequences have been well described in the literature and contain heptad repeat positioning for each amino acid. Coiled-coil nomenclature labels each of seven amino acids of a heptad repeat A through G, with amino acids A and D tending to be hydrophobic positions. Amino acids E and G tend to be charged. These four positions (A, D, E, and G) form the amphipathic backbone structure of a monomeric alpha-helix. The backbones of two or more amphipathic helices interact with each other to form di-, tri-, tetrameric, etc., coiled-coil structures.

In order to begin to design computer search motifs, a series of well characterized coiled coils were chosen including yeast transcription factor GCN4, Influenza Virus hemagglutinin loop 36, and human proto-oncogenes c-Myc, c-Fos, and c-Jun. For each peptide sequence, a strict homology for the A and D positions, and a list of the amino acids which could be excluded for the B, C, E, F, and G positions (because they are not observed in these positions) was determined. Motifs were tailored to the DP-107 and DP-178 sequences by deducing the most likely possibilities for heptad positioning of the amino acids of HIV-1 Bru DP-107, which is known to have coiled-coil structure, and HIV-1 Bru DP-178, which is still structurally undefined. The analysis of each of the sequences is contained in FIG. 12. For example, the motif for GCN4 was designed as follows:

1. The only amino acids (using standard single letter amino acid codes) found in the A or D positions of GCN4 were {LMNV}.
2. All amino acids were found at B, C, E, F, and G positions except {CFGIMPTW}.

3. The PESEARCH motif would, therefore, be written as follows:

[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)

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Translating or reading the motif: "at the first A position either L, M, N, or V must occur; at positions B and C (the next two positions) accept everything except C, F, G, I, M, P, T, or W; at the D position either L, M, N, or V must occur; at positions E, F, and G (the next 3 positions) accept everything except C, F, G, I, M, P, T, or W." This statement is contained four times in a 28-mer motif and five times in a 35-mer motif. The basic motif key then would be: [LMNV]-{CFGIMPTW}. The motif keys for the remaining well described coiled-coil sequences are summarized in FIG. 12.

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The motif design for DP-107 and DP-178 was slightly different than the 28-mer model sequences described above due to the fact that heptad repeat positions are not defined and the peptides are both longer than 28 residues. FIG. 13 illustrates several possible sequence alignments for both DP-107 and DP-178 and also includes motif designs based on 28^{mer}, 35^{mer}, and full-length peptides. Notice that only slight differences occur in the motifs as the peptides are lengthened. Generally, lengthening the base peptide results in a less stringent motif. This is very useful in broadening the possibilities for identifying DP-107-or DP-178-like primary amino acid sequences referred to in this document as "hits".

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In addition to making highly specific motifs for each type peptide sequence to be searched, it is also possible to make "hybrid" motifs. These motifs are

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made by "crossing" two or more very stringent motifs to make a new search algorithm which will find not only both "parent" motif sequences but also any peptide sequences which have similarities to one, the other, or both "parents". For example, in Table 3 the "parent" sequence of GCN4 is crossed with each of the possible "parent" motifs of DP-107. Now the hybrid motif must contain all of the amino acids found in the A and D positions of both parents, and exclude all of the amino acids not found in either parent at the other positions. The resulting hybrid from crossing GCN4 or [LMNV]{CFGIMPTW} and DP-107 (28-mer with the first L in the D position) or [ILQT]{CDFIMPST}, is [ILMNQTV]{CFIMPT}. Notice that now only two basic hybrid motifs exist which cover both framing possibilities, as well as all peptide lengths of the parent DP-107 molecule. FIG. 15 represents the hybridizations of GCN4 with DP-178. FIG. 16 represents the hybridizations of DP-107 and DP-178. It is important to keep in mind that the represented motifs, both parent and hybrid, are motif keys and not the depiction of the full-length motif needed to actually do the computer search.

Hybridizations can be performed on any combination of two or more motifs. Table 5 summarizes several three-motif hybridizations including GCN4, DP-107 (both frames), and DP-178 (also both frames). Notice that the resulting motifs are now becoming much more similar to each other. In fact, the first and third hybrid motifs are actually subsets of the second and fourth hybrid motifs respectively. This means that the first and third hybrid motifs are slightly more stringent than the second and fourth. It should also be noted that with only minor changes in these four motifs, or by hybridizing them, a single motif could be obtained

which would find all of the sequences. However, it should be remembered that stringency is also reduced. Finally, the most broad-spectra and least-stringent hybrid motif is described in FIG. 18 which summarizes the hybridization of GCN4, DP-107 (both frames), DP-178 (both frames), c-Fos, c-Jun, c-Myc, and Flu loop 36.

A special set of motifs was designed based on the fact that DP-178 is located only approximately ten amino acids upstream of the transmembrane spanning region of gp41 and just C-terminal to a proline which separates DP-107 and DP-178. It has postulated that DP-178 may be an amphipathic helix when membrane associated, and that the proline might aid in the initiation of the helix formation. The same arrangement was observed in Respiratory Syncytial Virus; however, the DP-178-like region in this virus also had a leucine zipper just C-terminal to the proline. Therefore, designed N-terminal proline-leucine zipper motifs were designed to analyze whether any other viruses might contain this same pattern. The motifs are summarized in FIG. 19.

The PC/Gene protein database contains 5879 viral amino acid sequences (library file PVIRUSES; CD-ROM release 11.0). Of these, 1092 are viral envelope or glycoprotein sequences (library file PVIRUSE1). Tables V through X contain lists of protein sequence names and motif hit locations for all the motifs searched.

**30 10. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
OF DP-107 AND DP-178-LIKE SEQUENCES
IN HUMAN IMMUNODEFICIENCY VIRUS**

FIG. 20 represents search results for HIV-1 BRU isolate gp41 (PC/Gene protein sequence PENV_HV1BR).

35 Notice that the hybrid motif which crosses DP-107 and

DP-178 (named 107x178x4; the same motif as found in FIG. 16 found three hits including amino acids 550-599, 636-688, and 796-823. These areas include DP-107 plus eight N-terminal and four C-terminal amino acids; DP-178 plus seven N-terminal and ten C-terminal amino acids; and an area inside the transmembrane region (cytoplasmic). FIG. 20 also contains the results obtained from searching with the motif named ALLMOTI5, for which the key is found in FIG. 17 ({CDGHP}{CFP}x5). This motif also found three hits including DP-107 (amino acids 510-599), DP-178 (615-717), and a cytoplasmic region (772-841). These hits overlap the hits found by the motif 107x178x4 with considerable additional sequences on both the amino and carboxy termini. This is not surprising in that 107x178x4 is a subset of the ALLMOTI5 hybrid motif. Importantly, even though the stringency of ALLMOTI5 is considerably less than 107x178x4, it still selectively identifies the DP-107 and DP-178 regions of gp41 shown to contain sequences for inhibitory peptides of HIV-1. The results of these two motif searches are summarized in Table V under the PC/Gene protein sequence name PENV HV1BR. The proline-leucine zipper motifs also gave several hits in HIV-1 BRU including 503-525 which is at the very C-terminus of gp120, just upstream of the cleavage site (P7LZIPC and P12LZIPC); and 735-768 in the cytoplasmic domain of gp41 (P23LZIPC). These results are found in Tables VIII, IX, and X under the same sequence name as mentioned above. Notice that the only area of HIV-1 BRU which is predicted by the Lupas algorithm to contain a coiled-coil region, is from amino acids 635-670. This begins eight amino acids N-terminal to the start and ends eight amino acids N-terminal to the end of DP-178. DP-107, despite the fact that it is a known coiled coil, is

not predicted to contain a coiled-coil region using the Lupas meth d.

11. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
OF DP-107-LIKE AND DP-178-LIKE
SEQUENCES IN HUMAN RESPIRATORY
SYNCTIAL VIRUS

FIG. 21 represents search results for Human Respiratory Syncytial Virus (RSV; Strain A2) fusion glycoprotein F1 (PC/Gene protein sequence name PVGLF_HRSVA). Motif 107x178x4 finds three hits including amino acids 152-202, 213-243, and 488-515. The arrangement of these hits is similar to what is found in HIV-1 except that the motif finds two regions with similarities to DP-178, one just downstream of what would be called the DP-107 region or amino acids 213-243, and one just upstream of the transmembrane region (also similar to DP-178) or amino acids 488-515. Motif ALLMOTI5 also finds three areas including amino acids 116-202, 267-302, and 506-549. The proline-leucine zipper motifs also gave several hits including amino acids 205-221 and 265-287 (P1LZIPC 265-280, P12LZIPC), and 484-513 (P7LZIPC and P12LZIPC 484-506, P23LZIPC). Notice that the PLZIP motifs also identify regions which share location similarities with DP-178 of HIV-1.

12. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES
IN SIMIAN IMMUNODEFICIENCY VIRUS

Motif hits for Simian immunodeficiency Virus gp41 (AGM3 isolate; PC/Gene protein sequence name PENV_SIVAG) are shown in FIG. 22. Motif 107x178x4 finds three hits including amino acids 566-593, 597-624, and 703-730. The first two hits only have three amino acids between them and could probably be combined into one hit from 566-624 which would

represent a DP-107-like hit. Amin acids 703 to 730 would then represent a DP-178-like hit. ALLMOTI5 also finds three hits including amino acids 556-628 (DP-107-like), 651-699 (DP-178-like), and 808-852 which represents the transmembrane spanning region. SIV
5 also has one region from 655-692 with a high propensity to form a coiled coil as predicted by the Lupas algorithm. Both 107x178x4 and ALLMOTI5 motifs find the same region. SIV does not have any PLZIP motif hits in gp41.

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13. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178 LIKE SEQUENCES
IN CANINE DISTEMPER VIRUS

Canine Distemper Virus (strain Onderstepoort)
15 fusion glycoprotein F1 (PC/Gene Protein sequence name PVGLF_CDVO) has regions similar to Human RSV which are predicted to be DP-107-like and DP-178-like (FIG. 23). Motif 107x178x4 highlights one area just C-terminal to the fusion peptide at amino acids 252-293. Amino
20 acids 252-286 are also predicted to be coiled coil using the Lupas algorithm. Almost 100 amino acids C-terminal to the first region is a DP-178-like area at residues 340-367. ALLMOTI5 highlights three areas of interest including: amino acids 228-297, which
25 completely overlaps both the Lupas prediction and the DP-107-like 107x178x4 hit; residues 340-381, which overlaps the second 107x178x4 hit; and amino acids 568-602, which is DP178-like in that it is located just N-terminal to the transmembrane region. It also
30 overlaps another region (residues 570-602) predicted by the Lupas method to have a high propensity to form a coiled coil. Several PLZIP motifs successfully identified areas of interest including P6 and P12LZIPC which highlight residues 336-357 and 336-361
35 respectively; P1 and P12LZIPC which find residues 398-

414; and P12 and P23LZIPC which find residues 562-589 and 562-592 respectively.

14. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES
IN NEWCASTLE DISEASE VIRUS

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FIG. 24 shows the motif hits found in Newcastle Disease Virus (strain Australia-Victoria/32; PC Gene protein sequence name PVGLF_NDVA). Motif 107x178x4 finds two areas including a DP-107-like hit at amino acids 151-178 and a DP-178-like hit at residues 426-512. ALLMOTI5 finds three areas including residues 117-182, 231-272, and 426-512. The hits from 426-512 include a region which is predicted by the Lupa method to have a high coiled-coil propensity (460-503). The PLZIP motifs identify only one region of interest at amino acids 273-289 (P1 and 12LZIPC).

15. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
OF DP-107-LIKE AND DP-178-LIKE
SEQUENCES IN HUMAN PARAINFLUENZA VIRUS

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Both motifs 107x178x4 and ALLMOTI5 exhibit DP-107-like hits in the same region, 115-182 and 117-182 respectively, of Human Parainfluenza Virus (strain NIH 47885; PC/Gene protein sequence name PVGLF_p13H4; (FIG. 25). In addition, the two motifs have a DP-178-like hit just slightly C-terminal at amino acids 207-241. Both motifs also have DP-178-like hits nearer the transmembrane region including amino acids 457-497 and 462-512 respectively. Several PLZIP motif hits are also observed including 283-303 (P5LZIPC), 283-310 (P12LZIPC), 453-474 (P6LZIPC), and 453-481 (P23LZIPC). The Lupa algorithm predicts that amino acids 122-176 have a propensity to form a coiled-coil.

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16. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES OF
INFLUENZA A VIRUS

FIG. 26 illustrates the Lupas prediction for a coiled coil in Influenza A Virus (strain A/Aichi/2/68) at residues 379-436, as well as the motif hits for 107x178x4 at amino acids 387-453, and for ALLMOT15 at residues 380-456. Residues 383-471 (38-125 of HA2) were shown by Carr and Kim to be an extended coiled coil when under acidic pH (Carr and Kim, 1993, Cell 73: 823-832). The Lupas algorithm predicts a coiled-coil at residues 379-436. All three methods successfully predicted the region shown to actually have coiled-coil structure; however, ALLMOT15 predicted the greatest portion of the 88 residue stretch.

17. EXAMPLE: RSV ANTIVIRAL COMPOUNDS

In the Example presented herein, respiratory syncytial virus (RSV) peptide sequences identified by utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit antiviral activity.

17.1 MATERIALS AND METHODS

Structural analyses consisted of circular dichroism (CD) studies, which were conducted according to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-RSV antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

A 48 amino acid RSV F2 peptide and a 53 amino acid RSV T67 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 21 for the exact position of these 5 sequences and for the motifs utilized.

17.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 48 amino acid RSV F2 peptide sequence (FIG. 27) and portions of the 53 amino acid RSV T67 peptide sequence (FIG. 28). The 10 oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-RSV activity. As shown in FIGS. 27 and 15 28, a number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

Thus, the computer assisted searches described, herein, in Example 9, for example, successfully 20 identified viral peptide domains that represent highly promising anti-RSV antiviral compounds.

18. EXAMPLE: HPF3 ANTIVIRAL COMPOUNDS

In the Example presented herein, human 25 parainfluenza virus 3 (HPF3) peptide sequences identified by utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit 30 antiviral activity.

18.1 MATERIALS AND METHODS

Structural analyses consisted of circular 35 dichroism (CD) studies, which were conducted according

to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-HPF3 antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

5 A 56 amino acid and 70 amino acid HPF3 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 25
10 for the exact positions of these sequences and for the motifs utilized.

18.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 56 amino acid HPF3 peptide sequence (FIG. 29) and portions of the 70 amino acid HPF3 peptide sequence (FIG. 30). The oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-HPF3 activity. As shown in FIGS. 29 and 30, a
20 number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

Thus, the computer assisted searches described, herein, in Example 9, for example, successfully
25 identified viral peptide domains that represent highly promising anti-HPF3 antiviral compounds.

The present invention is not to be limited in scope by the specific embodiments described which are intended as single illustrations of individual aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various modifications of the invention, in addition to those shown and described herein will
35 become apparent to those skilled in the art from the

foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

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WHAT IS CLAIMED IS:

1. A peptide having an amino acid sequence corresponding to an α -helix region of an extracellular domain of a viral envelope protein, which interacts with and binds to a second α -helix region of the viral envelope protein containing a leucine-zipper domain having a coiled-coil structure.
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2. The peptide of Claim 1 wherein the peptide is recognized by a computer-assisted peptide sequence search utilizing an ALLMOTI5, 107x178x4 motif, or a PLZIP motif.
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3. The peptide of Claim 1 in which the enveloped virus is a retrovirus.
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4. The peptide of Claim 3 in which the retrovirus is a human retrovirus.
- 20 5. The peptide of Claim 4 in which the human retrovirus is HIV-1 or HIV-2.
- 25 6. The peptide of Claim 4 in which the human retrovirus is HTLV-I or HTLV-II
7. The peptide of Claim 1 in which the enveloped virus is a non-human retrovirus.
- 30 8. The peptide of Claim 6 in which the non-human retrovirus is bovine leukosis virus, feline sarcoma virus, feline leukemia virus, simian immunodeficiency virus, simian sarcoma virus, and sheep progress pneumonia virus.

9. The peptide of Claim 1 in which the enveloped virus is a non-retroviral virus.

10. The peptide of Claim 9 in which the virus is respiratory syncytial virus, influenza virus,
5 parainfluenza virus, canine distemper virus, or newcastle disease virus.

11. A peptide having a formula selected from the group consisting of:

- 10 X-YTS-Z
 X-YTSL-Z
 X-YTSLI-Z
 X-YTSLIH-Z
 X-YTSLIHS-Z
 X-YTSLIHSZ
 X-YTSLIHSLI-Z
15 X-YTSLIHSLIE-Z
 X-YTSLIHSLIEE-Z
 X-YTSLIHSLIEES-Z
 X-YTSLIHSLIEESQ-Z
 X-YTSLIHSLIEESQN-Z
 X-YTSLIHSLIEESQNQ-Z
 X-YTSLIHSLIEESQNQQ-Z
20 X-YTSLIHSLIEESQNQQE-Z
 X-YTSLIHSLIEESQNQQEK-Z
 X-YTSLIHSLIEESQNQQEKN-Z
 X-YTSLIHSLIEESQNQQEKNE-Z
 X-YTSLIHSLIEESQNQQEKNEQ-Z
 X-YTSLIHSLIEESQNQQEKNEQEL-Z
 X-YTSLIHSLIEESQNQQEKNEQELL-Z
25 X-YTSLIHSLIEESQNQQEKNEQELLE-Z
 X-YTSLIHSLIEESQNQQEKNEQELLEL-Z
 X-YTSLIHSLIEESQNQQEKNEQELLED-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDK-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKW-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKWA-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKWAS-Z
30 X-YTSLIHSLIEESQNQQEKNEQELLDKWASL-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKWASLW-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKWASLWN-Z
 X-YTSLIHSLIEESQNQQEKNEQELLDKWASLWNW-Z and
 X-YTSLIHSLIEESQNQQEKNEQELLDKWASLWNWF-Z (SEQ ID:1), or

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X-NWF-Z
 X-WNWF-Z
 X-LWNWF-Z
 X-SLWNWF-Z
 X-ASLWNWF-Z
 X-WASLWNWF-Z
 X-KWASLWNWF-Z
 X-DKWASLWNWF-Z
 X-LDKWASLWNWF-Z
 X-ELDKWASLWNWF-Z
 X-LELDKWASLWNWF-Z
 X-LLELDKWASLWNWF-Z
 X-ELLELDKWASLWNWF-Z
 X-QELLELDKWASLWNWF-Z
 X-EQELLELDKWASLWNWF-Z
 X-NEQELLELDKWASLWNWF-Z
 X-KNEQELLELDKWASLWNWF-Z
 X-EKNEQELLELDKWASLWNWF-Z
 X-QEKNEQELLELDKWASLWNWF-Z
 X-QQEKNEQELLELDKWASLWNWF-Z
 X-NQQEKNEQELLELDKWASLWNWF-Z
 X-QNQQEKNEQELLELDKWASLWNWF-Z
 X-SQNQQEKNEQELLELDKWASLWNWF-Z
 X-ESQNQQEKNEQELLELDKWASLWNWF-Z
 X-EESQNQQEKNEQELLELDKWASLWNWF-Z
 X-IEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-LIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-SLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 and X-TSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z

in which:

25 amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluorenylmethoxy-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

30 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

35 12. A peptide having a formula selected from the group consisting of:

X-LEA-Z
 X-LEAN-Z
 X-LEANI-Z
 X-LEANIS-Z
 X-LEANISQ-Z
 X-LEANISQS-Z
 X-LEANISSQL-Z
5 X-LEANISQSLE-Z
 X-LEANISQSLEQ-Z
 X-LEANISQSLEQA-Z
 X-LEANISQSLEQAQ-Z
 X-LEANISQSLEQAQI-Z
 X-LEANISQSLEQAQIQ-Z
 X-LEANISQSLEQAQIQQ-Z
10 X-LEANISQSLEQAQIQQE-Z
 X-LEANISQSLEQAQIQQEKN-Z
 X-LEANISQSLEQAQIQQEKNM-Z
 X-LEANISQSLEQAQIQQEKNMY-Z
 X-LEANISQSLEQAQIQQEKNMYE-Z
 X-LEANISQSLEQAQIQQEKNMYEL-Z
 X-LEANISQSLEQAQIQQEKNMYELQ-Z
15 X-LEANISQSLEQAQIQQEKNMYELQK-Z
 X-LEANISQSLEQAQIQQEKNMYELQKL-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-S-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SW-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWD-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDV-Z
20 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVF-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFT-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTN-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTNW-Z and
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTNWL-Z (SEQ ID: 7), or

25
 X-NWL-Z
 X-TNWL-Z
 X-FTNWL-Z
 X-VFTNWL-Z
 X-DVFTNWL-Z
 X-WDVFTNWL-Z
 X-SWDVFTNWL-Z
 X-NSWDVFTNWL-Z
 X-LNSWDVFTNWL-Z
 X-KLNSWDVFTNWL-Z
 X-QKLNSWDVFTNWL-Z
 X-LQKLNSWDVFTNWL-Z
 X-ELQKLNSWDVFTNWL-Z
 X-YELQKLNSWDVFTNWL-Z
 X-MYELQKLNSWDVFTNWL-Z
 X-NMYELQKLNSWDVFTNWL-Z
 X-KNMYELQKLNSWDVFTNWL-Z
30
 X-EKNMYELQKLNSWDVFTNWL-Z
 X-QEKNMYELQKLNSWDVFTNWL-Z

35

X-QQEKNMYELQKLNSWDVFTNWL-Z
 X-IQQEKNMYELQKLNSWDVFTNWL-Z
 X-QIQQEKNMYELQKLNSWDVFTNWL-Z
 X-AQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 5 X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QKSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-SQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 and X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

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in which:

amino acid residues are presented by the single-letter code;

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X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

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Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

13. A peptide having a formula selected from the group consisting of:

X-YTS-Z
 X-YTSV-Z
 25 X-YTSVI-Z
 X-YTSVIT-Z
 X-YTSVITI-Z
 X-YTSVITIE-Z
 X-YTSVITIEL-Z
 X-YTSVITIELS-Z
 X-YTSVITIELSN-Z
 30 X-YTSVITIELSNI-Z
 X-YTSVITIELSNIK-Z
 X-YTSVITIELSNIKE-Z
 X-YTSVITIELSNIKEN-Z
 X-YTSVITIELSNIKENK-Z
 X-YTSVITIELSNIKENKC-Z
 X-YTSVITIELSNIKENKCN-Z
 X-YTSVITIELSNIKENKCNG-Z
 35 X-YTSVITIELSNIKENKNGT-Z
 X-YTSVITIELSNIKENKNGTD-Z

X-YTSVITIELSNIKENCNGTDA-Z
 X-YTSVITIELSNIKENCNGTDAK-Z
 X-YTSVITIELSNIKENCNGTDAKV-Z
 X-YTSVITIELSNIKENCNGTDAVK-Z
 X-YTSVITIELSNIKENCNGTDAVKL-Z
 X-YTSVITIELSNIKENCNGTDAVKLI-Z
 X-YTSVITIELSNIKENCNGTDAVKLIK-Z
5 X-YTSVITIELSNIKENCNGTDAVKLIKQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQE-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQEL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELD-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDK-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKY-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYK-Z
10 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKN-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNA-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAV-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVT-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTE-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTEL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQL-Z
15 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLLM-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLMQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLMQS-Z and
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLMQST-Z, or

X-QST-Z
 X-MQST-Z
 X-LMQST-Z
 X-LLMQST-Z
 X-QLLMQST-Z
 X-LQLLMQST-Z
 X-ELQLLMQST-Z
 X-TELQLLMQST-Z
 X-VTELQLLMQST-Z
20 X-AVTELQLLMQST-Z
 X-NAVTELQLLMQST-Z
 X-KNAVTELQLLMQST-Z
 X-YKNAVTELQLLMQST-Z
 X-KYKNAVTELQLLMQST-Z
 X-DKYKNAVTELQLLMQST-Z
 X-LDKYKNAVTELQLLMQST-Z
 X-ELDKYKNAVTELQLLMQST-Z
25 X-QELEDKYKNAVTELQLLMQST-Z
 X-KQELEDKYKNAVTELQLLMQST-Z
 X-IKQELEDKYKNAVTELQLLMQST-Z
 X-LIKQELEDKYKNAVTELQLLMQST-Z
 X-KLIKQELEDKYKNAVTELQLLMQST-Z
 X-VKLIKQELEDKYKNAVTELQLLMQST-Z
 X-KVKLIKQELEDKYKNAVTELQLLMQST-Z
30 X-AKVKLIKQELEDKYKNAVTELQLLMQST-Z
 X-DAKVKLIKQELEDKYKNAVTELQLLMQST-Z

X-QST-Z
 X-MQST-Z
 X-LMQST-Z
 X-LLMQST-Z
 X-QLLMQST-Z
 X-LQLLMQST-Z
 X-ELQLLMQST-Z
 X-TELQLLMQST-Z
 X-VTELQLLMQST-Z
 X-AVTELQLLMQST-Z
 X-NAVTELQLLMQST-Z
 X-KNAVTELQLLMQST-Z
 X-YKNAVTELQLLMQST-Z
 X-KYKNAVTELQLLMQST-Z
 X-DKYKNAVTELQLLMQST-Z
 X-LDKYKNAVTELQLLMQST-Z
 X-ELDKYKNAVTELQLLMQST-Z
35 X-QELEDKYKNAVTELQLLMQST-Z
 X-KQELEDKYKNAVTELQLLMQST-Z
 X-IKQELEDKYKNAVTELQLLMQST-Z
 X-LIKQELEDKYKNAVTELQLLMQST-Z
 X-KLIKQELEDKYKNAVTELQLLMQST-Z
 X-VKLIKQELEDKYKNAVTELQLLMQST-Z
 X-KVKLIKQELEDKYKNAVTELQLLMQST-Z
 X-AKVKLIKQELEDKYKNAVTELQLLMQST-Z
 X-DAKVKLIKQELEDKYKNAVTELQLLMQST-Z

X-TDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-GTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-CNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-KCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 5 X-KENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-IKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-SNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-LSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 10 X-TIELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ITIELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-VITIELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-SVITIELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z
 X-TSVITIELSNIKENKCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z

in which:

15 amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

20 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

25 14. A peptide having a formula selected from the group consisting of:

X-FYD-Z
 X-FYDP-Z
 X-FYDPL-Z
 X-FYDPLV-Z
 X-FYDPLVF-Z
 30 X-FYDPLVFP-Z
 X-FYDPLVFPS-Z
 X-FYDPLVFPsd-Z
 X-FYDPLVFPsDE-Z
 X-FYDPLVFPsDEF-Z
 X-FYDPLVFPsDEFd-Z
 X-FYDPLVFPsDEFdA-Z
 35 X-FYDPLVFPsDEFdAs-Z
 X-FYDPLVFPsDEFdAsI-Z

X-FYDPLVFPSDEFDA SIS-Z
 X-FYDPLVFPSDEFDA SISQ-Z
 X-FYDPLVFPSDEFDA SISQV-Z
 X-FYDPLVFPSDEFDA SISQVN-Z
 X-FYDPLVFPSDEFDA SISQVNE-Z
 X-FYDPLVFPSDEFDA SISQVNEK-Z
 X-FYDPLVFPSDEFDA SISQVNEKI-Z
5 X-FYDPLVFPSDEFDA SISQVNEKIN-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQ-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQS-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSL-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLA-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAF-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFI-Z
10 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIR-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIR-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIRKS-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIRKS-D-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIRKSDE-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIRKSDEL-Z
 X-FYDPLVFPSDEFDA SISQVNEKINQSLAFIRKSDELL-Z, or

15 X-DELL-Z
 X-SDELL-Z
 X-KSDELL-Z
 X-RKSDELL-Z
 X-IRKSDELL-Z
 X-FIRKSDELL-Z
 X-AFIRKSDELL-Z
 X-LAFIRKSDELL-Z
20 X-SLAFIRKSDELL-Z
 X-QSLAFIRKSDELL-Z
 X-NQSLAFIRKSDELL-Z
 X-INQSLAFIRKSDELL-Z
 X-KINQSLAFIRKSDELL-Z
 X-EKINQSLAFIRKSDELL-Z
 X-NEKINQSLAFIRKSDELL-Z
25 X-VNEKINQSLAFIRKSDELL-Z
 X-QVNEKINQSLAFIRKSDELL-Z
 X-SQVNEKINQSLAFIRKSDELL-Z
 X-ISQVNEKINQSLAFIRKSDELL-Z
 X-SISQVNEKINQSLAFIRKSDELL-Z
 X-ASISQVNEKINQSLAFIRKSDELL-Z
 X-DASISQVNEKINQSLAFIRKSDELL-Z
30 X-FDASISQVNEKINQSLAFIRKSDELL-Z
 X-EFDASISQVNEKINQSLAFIRKSDELL-Z
 X-DEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-SDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-PSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-FPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-VFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-LVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
35 X-PLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-DPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

X-YDPLVFFSDEFDASISQVNEKINQSLAFIRKSDELL-Z

in which:

amino acid residues are presented by the single-letter code;

- 5 X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;
- 10 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

15. A peptide having a formula selected from the
15 group consisting of:

- 15 X-ITL-Z
X-ITLN-Z
X-ITLNN-Z
X-ITLNNS-Z
X-ITLNNSV-Z
X-ITLNNSVA-Z
20 X-ITLNNSVAL-Z
X-ITLNNSVALD-Z
X-ITLNNSVALDP-Z
X-ITLNNSVALDPI-Z
X-ITLNNSVALDPID-Z
X-ITLNNSVALDPIDI-Z
X-ITLNNSVALDPIDIS-Z
X-ITLNNSVALDPIDISI-Z
25 X-ITLNNSVALDPIDISIE-Z
X-ITLNNSVALDPIDISIEL-Z
X-ITLNNSVALDPIDISIELN-Z
X-ITLNNSVALDPIDISIELNK-Z
X-ITLNNSVALDPIDISIELNKA-Z
X-ITLNNSVALDPIDISIELNKA-K-Z
X-ITLNNSVALDPIDISIELNKA-KS-Z
X-ITLNNSVALDPIDISIELNKA-KSD-Z
30 X-ITLNNSVALDPIDISIELNKA-KSDL-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-E-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-E-E-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-EES-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-EESKE-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-EESKEW-Z
35 X-ITLNNSVALDPIDISIELNKA-KSDL-EESKEWI-Z
X-ITLNNSVALDPIDISIELNKA-KSDL-EESKEWIR-Z

X-ITLNNSVALDPIDISIELNKAKSLEESKEWIRR-Z
 X-ITLNNSVALDPIDISIELNKAKSLEESKEWIRRS-Z, or

	X-RRS-Z
	X-IRRS-Z
	X-WIRRS-Z
5	X-EWIRRS-Z
	X-KEWIRRS-Z
	X-SKEWIRRS-Z
	X-ESKEWIRRS-Z
	X-EESKEWIRRS-Z
	X-LEESKEWIRRS-Z
	X-DLEESKEWIRRS-Z
	X-SDLEESKEWIRRS-Z
10	X-KSDLEESKEWIRRS-Z
	X-AKSDLEESKEWIRRS-Z
	X-KAKSDLEESKEWIRRS-Z
	X-NKAKSDLEESKEWIRRS-Z
	X-LNKAKSLEESKEWIRRS-Z
	X-ELNKAKSLEESKEWIRRS-Z
	X-IELNKAKSLEESKEWIRRS-Z
	X-SIELNKAKSLEESKEWIRRS-Z
15	X-ISIELNKAKSLEESKEWIRRS-Z
	X-DISIELNKAKSLEESKEWIRRS-Z
	X-IDISIELNKAKSLEESKEWIRRS-Z
	X-PIDISIELNKAKSLEESKEWIRRS-Z
	X-DPIDISIELNKAKSLEESKEWIRRS-Z
	X-LDPIDISIELNKAKSLEESKEWIRRS-Z
	X-ALDPIDISIELNKAKSLEESKEWIRRS-Z
20	X-VALDPIDISIELNKAKSLEESKEWIRRS-Z
	X-SVALDPIDISIELNKAKSLEESKEWIRRS-Z
	X-NSVALDPIDISIELNKAKSLEESKEWIRRS-Z
	X-NNNSVALDPIDISIELNKAKSLEESKEWIRRS-Z
	X-LNNNSVALDPIDISIELNKAKSLEESKEWIRRS-Z
	X-TLNNNSVALDPIDISIELNKAKSLEESKEWIRRS-Z

in which:

25	amino acid residues are presented by the single-letter code;
	X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;
30	Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

35

16. A peptide having a formula selected from the group consisting of:

X-ALG-Z

X-ALGV-Z

X-ALGVA-Z

X-ALGVAT-Z

5 X-ALGVATS-Z

X-ALGVATSA-Z

X-ALGVATSAQ-Z

X-ALGVATSAQI-Z

X-ALGVATSAQIT-Z

X-ALGVATSAQITA-Z

X-ALGVATSAQITAA-Z

10 X-ALGVATSAQITAAV-Z

X-ALGVATSAQITAAVA-Z

X-ALGVATSAQITAAVAL-Z

X-ALGVATSAQITAAVALV-Z

X-ALGVATSAQITAAVALVE-Z

X-ALGVATSAQITAAVALVEA-Z

X-ALGVATSAQITAVALVEAK-Z

X-ALGVATSAQITAVALVEAKQ-Z

15 X-ALGVATSAQITAVALVEAKQA-Z

X-ALGVATSAQITAVALVEAKQAR-Z

X-ALGVATSAQITAVALVEAKQARS-Z

X-ALGVATSAQITAVALVEAKQARSD-Z

X-ALGVATSAQITAVALVEAKQARSDI-Z

X-ALGVATSAQITAVALVEAKQARSDIE-Z

X-ALGVATSAQITAVALVEAKQARS DIEK-Z

20 X-ALGVATSAQITAVALVEAKQARS DIEKL-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLK-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLKE-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLKEA-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLKEAI-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLKEAIR-Z

X-ALGVATSAQITAVALVEAKQARS DIEKLKEAIRD-Z, or

25

X-IRD-Z

X-AIRD-Z

X-EAIRD-Z

X-KEAIRD-Z

X-LKEAIRD-Z

X-KLKEAIRD-Z

X-EKLKEAIRD-Z

X-IEKLKEAIRD-Z

X-DIEKLKEAIRD-Z

X-SDIEKLKEAIRD-Z

X-RSDIEKLKEAIRD-Z

X-ARS DIEKLKEAIRD-Z

X-QARS DIEKLKEAIRD-Z

X-KQARS DIEKLKEAIRD-Z

X-AKQARS DIEKLKEAIRD-Z

X-EAKQARS DIEKLKEAIRD-Z

30 X-VEAKQARS DIEKLKEAIRD-Z

35

X-LVEAKQARS DIEKLKEAIRD-Z
X-ALVEAKQARS DIEKLKEAIRD-Z
X-VALVEAKQARS DIEKLKEAIRD-Z
X-AVALVEAKQARS DIEKLKEAIRD-Z
X-AAVALVEAKQARS DIEKLKEAIRD-Z
X-TAAVALVEAKQARS DIEKLKEAIRD-Z
X-ITAVALVEAKQARS DIEKLKEAIRD-Z
5 X-QITAVALVEAKQARS DIEKLKEAIRD-Z
X-AQITAVALVEAKQARS DIEKLKEAIRD-Z
X-SAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-TSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-ATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-VATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
10 X-GVATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-LGVATSAQITAVALVEAKQARS DIEKLKEAIRD-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethyoxyethyl-carbonyl group, a hydrophobic group, or a macromolecular carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

17. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein **X** is a hydrophobic group.

25 **18.** The peptide of Claim 17 wherein the hydrophobic group **X** is carbobenzoyl, dansyl, or t-butyloxycarbonyl.

30 **19.** The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein **Z** is a hydrophobic group.

20. The peptide of Claim 19 wherein the hydrophobic group **Z** is t-butyloxycarbonyl.

21. The peptide of Claim 11, 12, 13, 14, 15 or
16 wherein X is a macromolecular carrier group.

22. The peptide of Claim 21 wherein the
macromolecular carrier group is a lipid-fatty acid
5 conjugate, a polyethylene glycol, or a carbohydrate
moiety.

23. The peptide of Claim 11, 12, 13, 14, 15 or
16 wherein Z is a macromolecular carrier group.
10

24. The peptide of Claim 23 wherein the
macromolecular carrier group Z is a lipid-fatty acid
conjugate, a polyethylene glycol, or a carbohydrate
moiety.
15

25. The peptide of Claim 11, 12, 13, 14, 15 or
16 wherein at least one bond linking adjacent amino
acid residues is a non-peptide bond.

20 26. The peptide of Claim 25 wherein the non-
peptide bond is an imino, ester, hydrazine,
semicarbazide, or azo bond.

25 27. The peptide of Claim 11, 12, 13, 14, 15 or
16 wherein at least one amino acid residue is in a D-
isomer configuration.

28. The peptide of Claim 11, 12, 13, 14, 15 or
16 further comprising at least one amino acid
30 insertion.

29. The peptide of Claim 11, 12, 13, 14, 15 or
16 wherein the amino acid insertion is between 1 and
15 amino acid residues.
35

30. The peptide of Claim 11, 12, 13, 14, 15 or
16 having at least one less amino acid residue,
wherein the amino acid residue(s) represents an amino
acid deletion, and wherein the peptide comprises at
least three amino acid residues.

5

31. The peptide of Claim 11, 12, 13, 14, 15 or
16 further comprising at least one amino acid
substitution wherein a first amino acid residue is
substituted for a second, different amino acid
10 residue.

32. The peptide of Claim 31 wherein the amino
acid substitution is a conserved substitution.

15

33. The peptide of Claim 31 wherein the amino
acid substitution is a non-conserved substitution.

20

34. A method for the inhibition of transmission
of an enveloped virus to a cell, comprising contacting
the cell with an effective concentration of the
peptide of Claim 1 for an effective period of time so
that no infection of the cell by the virus occurs.

25

35. A method for neutralizing an enveloped virus
in a host, comprising administering to the host an
effective concentration of the peptide of Claim 1 so
that the host raises an immune response sufficient to
neutralize the virus, and viral infection of
uninfected cells in the host is inhibited.

30

36. A method for neutralizing an enveloped virus
in a host, comprising administering to the host an
effective concentration of an antibody raised against
the peptide of Claim 1 so that viral infection of
35 uninfected cells in the host is inhibited.

37. A method for the detection of an enveloped virus comprising:

5 contacting a viral isolate with an effective concentration of the peptide of Claim 1 for an effective amount of time so that viral infectivity is inhibited; and

assaying the viral isolate for viral enzyme activity.

38. A method for the inhibition of transmission 10 of an HIV retrovirus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 11 or 12 for an effective period of time so that no infection of the cell by the retrovirus occurs.

15

39. A method for neutralizing an HIV retrovirus 20 in a host, comprising administering to the host an effective concentration of the peptide of Claim 11 or 12 so that the host raises an immune response sufficient to neutralize the HIV retrovirus, and HIV infection of uninfected cells in the host is inhibited.

40. A method for neutralizing an HIV retrovirus 25 in a host, comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 11 or 12 so that HIV infection of uninfected cells in the host is inhibited.

30

41. A method for the detection of HIV, comprising:

35 contacting a viral isolate with an effective concentration of the peptide of Claim 11 or 12 for an effective amount of time so that HIV viral infectivity is inhibited; and

assaying the viral isolat for retroviral enzyme activity.

42. A method for the inhibition of transmission of a respiratory syncytial virus to a cell, comprising
5 contacting the cell with an effective concentration of the peptide of Claim 13 or 14 for an effective period of time so that no infection of the cell by the virus occurs.

10 43. A method for neutralizing a respiratory syncytial virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 13 or 14 so that the host raises an immune response sufficient to neutralize the virus, and
15 respiratory syncytial virus infection of uninfected cells in the host is inhibited.

20 44. A method for neutralizing a respiratory syncytial virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 13 or 14 so that respiratory syncytial virus infection of uninfected cells in the host is inhibited.

25 45. A method for the detection of respiratory syncytial virus comprising:
contacting a viral isolate with an effective concentration of the peptide of Claim 13 or 14 for an effective amount of time so that respiratory syncytial
30 viral infectivity is inhibited; and
assaying the viral isolate for respiratory syncytial virus enzyme activity.

35 46. A method for the inhibition of transmission of a parainfluenza virus to a cell comprising,

contacting the cell with an effective concentration of the peptide of Claim 15 or 16 for an effective period of time so that no infection of the cell by the virus occurs.

5 47. A method for neutralizing a parainfluenza virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 15 or 16 so that the host raises an immune response sufficient to neutralize the virus, and parainfluenza
10 infection of uninfected cells in the host is inhibited.

15 48. A method for neutralizing a parainfluenza virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 15 or 16 so that parainfluenza infection of uninfected cells in the host is inhibited.

20 49. A method for the detection of parainfluenza virus comprising:

25 contacting a viral isolate with an effective concentration of the peptide of Claim 15 or 16 for an effective amount of time so that parainfluenza viral infectivity is inhibited; and

assaying the viral isolate for parainfluenza virus enzyme activity.

30

35

HIV1LAI (DP-178; SEQ ID:1)	YTSLIHSLEEQQEKENQEELLELDKWA SLWNWF
HIV1SF2 (DP-185; SEQ ID:3)	YTNTIYNLLEESQQEKENQEELLELDKWA SLWNWF
HIV1RF (SEQ ID:4)	YTGIIYNLLEESQQEKENQEELLELDKWA NLWNWF
HIV1MN (SEQ ID:5)	YTSLIYSLLEKSQTQQEKENQEELLELDKWA SLWNWF
HIV2R0D (SEQ ID:6)	LEANISKSLEQAAQIQEQKNMYELQKLN SMWIFGNWF
HIV2NIHZ (SEQ ID:7)	LEANISQSLEQAAQIQEQKNMYELQKLN SMWIFGNWF
DP180 (SEQ ID:2)	SSESF TLLEQWNNMKLQLAEQWML EQINEKHYLEDIS
DP118 (SEQ ID:10)	QQLDVWKRRQEMRLTWGTKNL QARVTAEKYLKQDQ
DP125 (SEQ ID:8)	CGGNNLLRAIEAQQHLLQL TVWG IKQLQARI LAVERYLKQDQ
DP116 (SEQ ID:9)	LQARIL AVERYLKQDQ

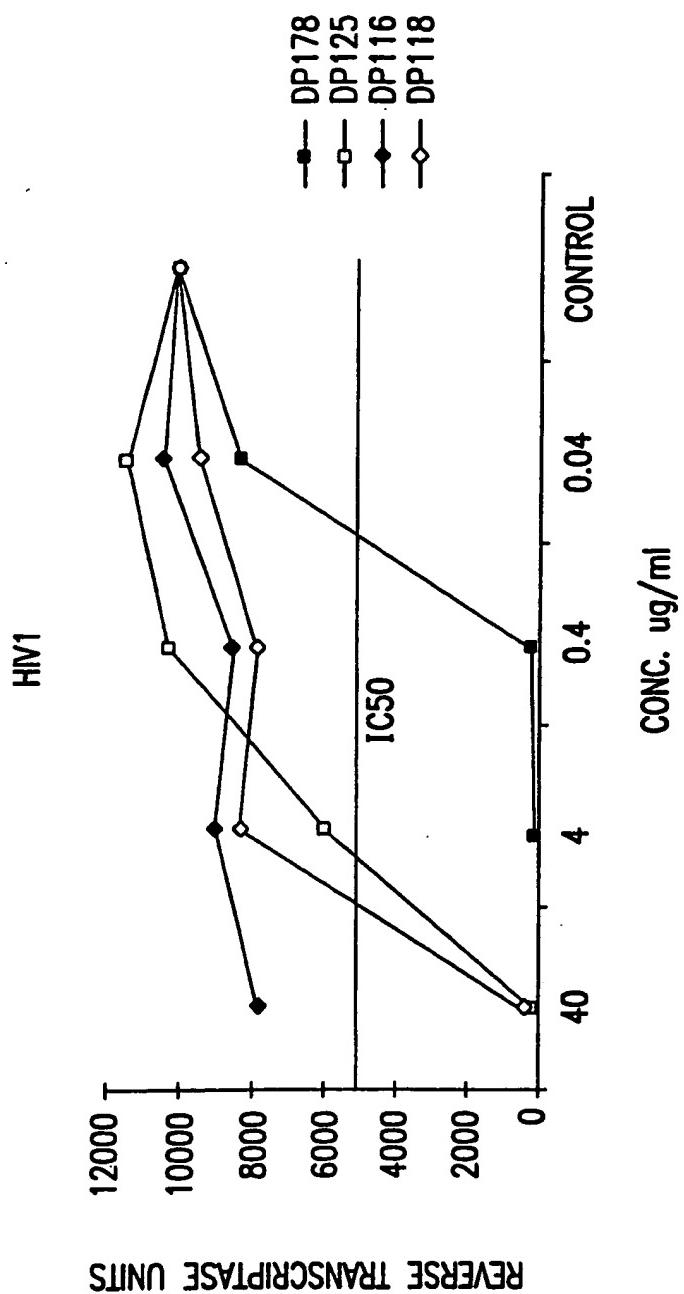


FIG.2

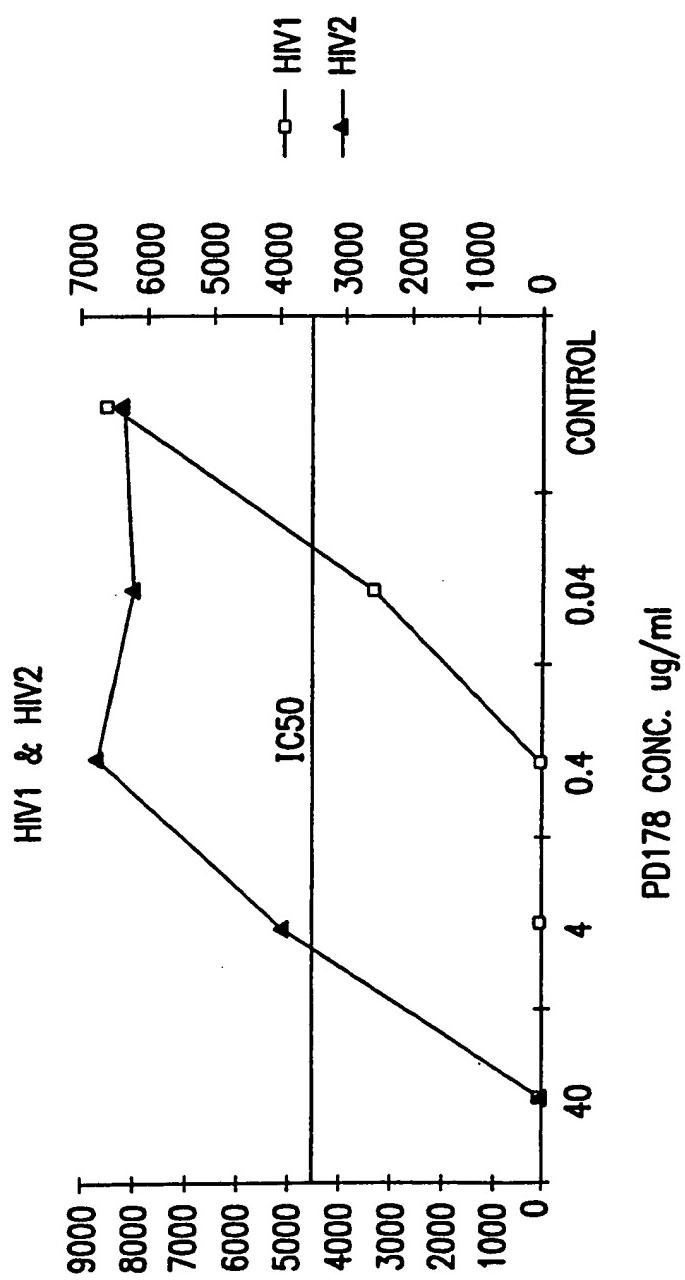


FIG. 3

3 / 31

<u>Number of Syncytia/well: concentration in µg/ml (micrograms/ml)</u>										
DP178	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control	
<i>Syncytia</i>										
HIV1LAI	0	0	0	0	0	0	0	0	67	
HIV1MN	0	0	0	0	0	ND	ND	ND	34	
HIV1RF	0	0	0	0	0	ND	ND	ND	65	
HIV1SF2	0	0	0	0	0	ND	ND	ND	58	
DP125	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control	
<i>Syncytia</i>										
HIV1LAI	0	0	54	69	80	75	79	82	67	
HIV1MN	0	0	30	36	ND	ND	ND	ND	34	
HIV1RF	0	0	67	63	ND	ND	ND	ND	65	
HIV1SF2	0	0	9	66	ND	ND	ND	ND	58	
DP116	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control	
<i>Syncytia</i>										
HIV1LAI	75	ND	ND	ND	ND	ND	ND	ND	67	
HIV1MN	35	ND	ND	ND	ND	ND	ND	ND	34	
HIV1RF	81	ND	ND	ND	ND	ND	ND	ND	65	
HIV1SF2	81	ND	ND	ND	ND	ND	ND	ND	58	

FIG.4A

DP180	40	20	10	5	2.5	1.25	0.625	0.3125	Control	
<i>Syncytia</i>										
HIV1LAI	50	>45	>45	>45	>45	>45	>45	>45	58	
DP185	40	20	10	5	2.5	1.25	0.625	0.3125	Control	
<i>Syncytia</i>										
HIV1LAT	0	0	0	0	0	0	0	ND	60	

FIG.4B

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<u>HIV1</u>								
<u>Number of Syncytia/well: concentration in ng/ml (nanograms/ml)</u>								
DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV1	0	0	0	0	0	14	20	48
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV1	ND	48	ND	ND	ND	ND	ND	ND
<u>HIV2</u>								
<u>Number of Syncytia/well: concentration in µg/ml (micrograms/ml)</u>								
DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV2	50	54	55	57	63	77	78	76
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV2	ND	58	ND	ND	ND	ND	ND	ND

FIG.5

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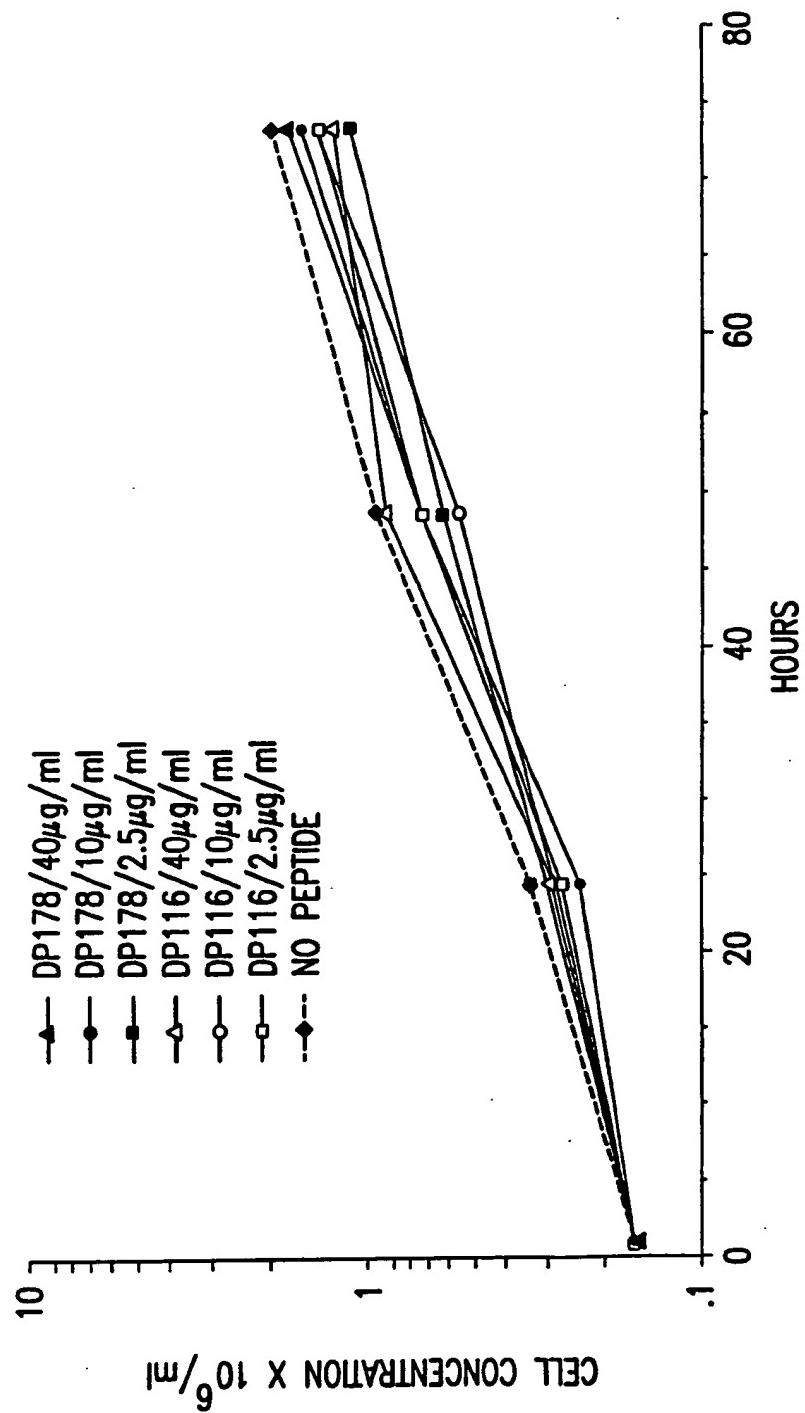
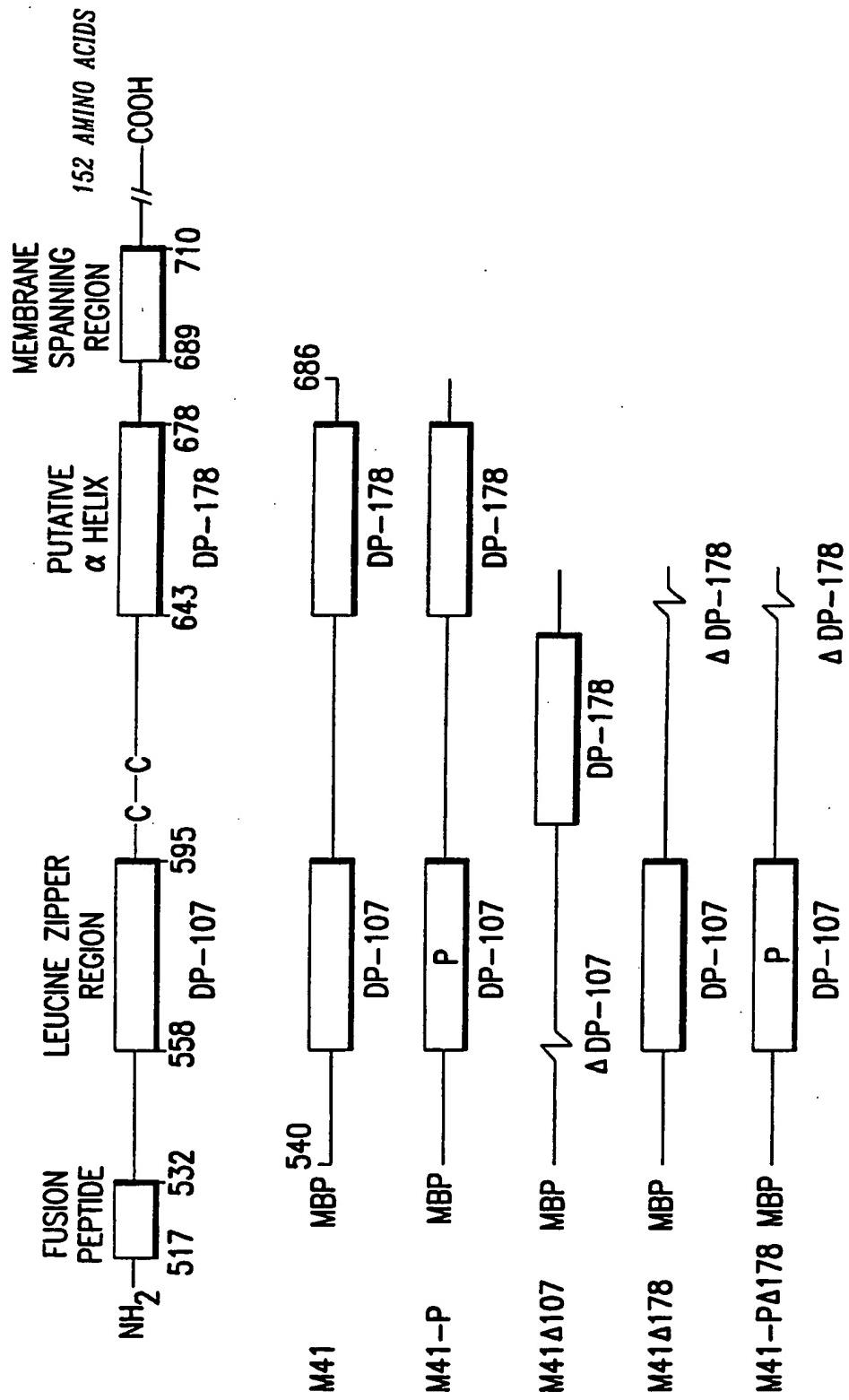


FIG. 6



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FIG. 7

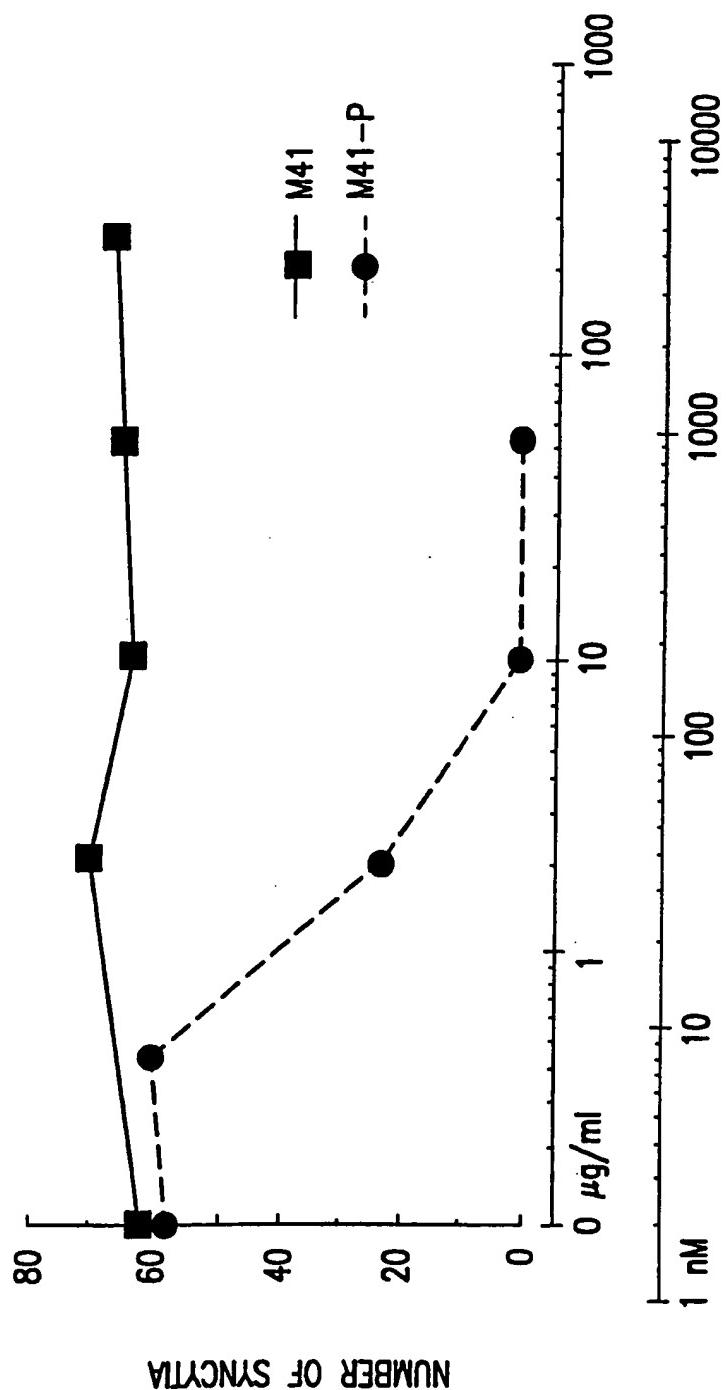


FIG. 8

NUMBER OF SYNCYTIA

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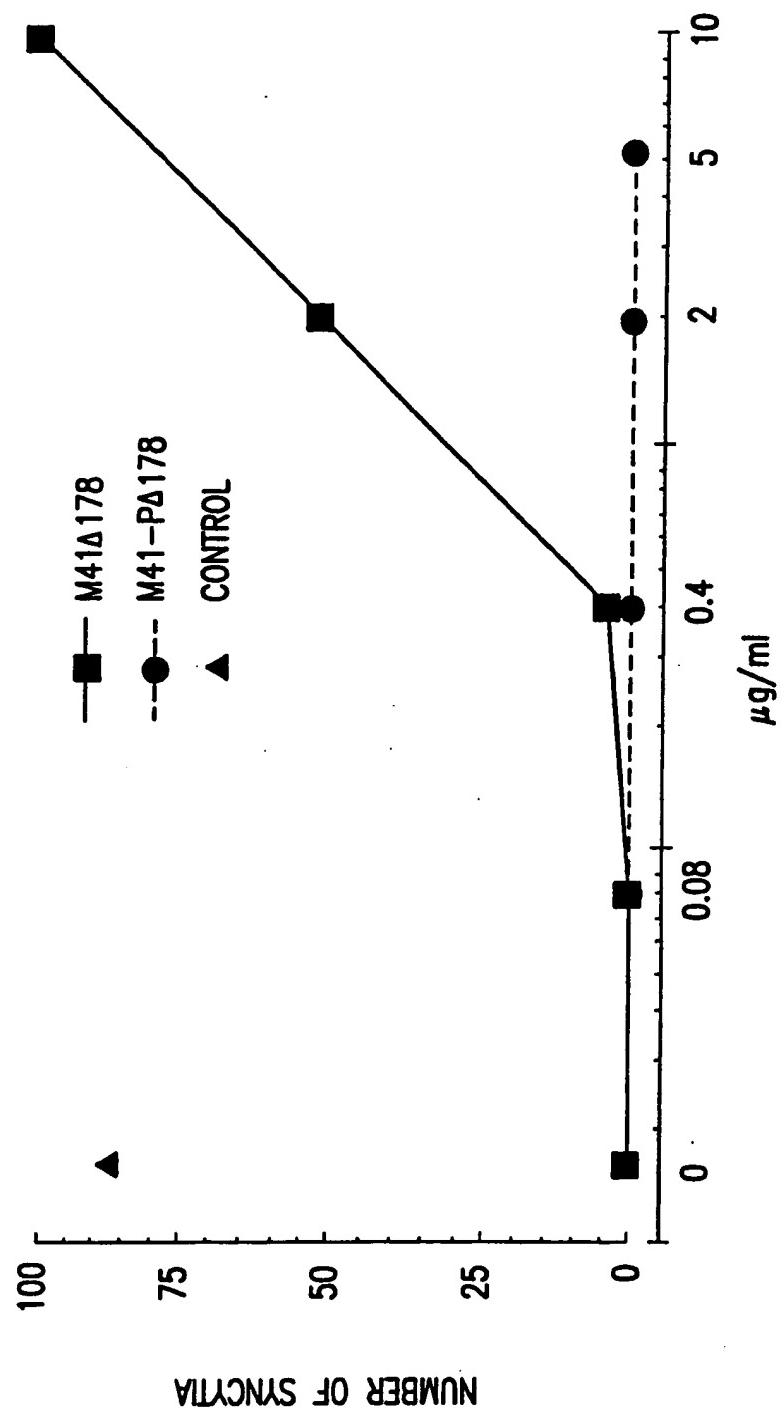


FIG. 9

NUMBER OF SYNCYTIA

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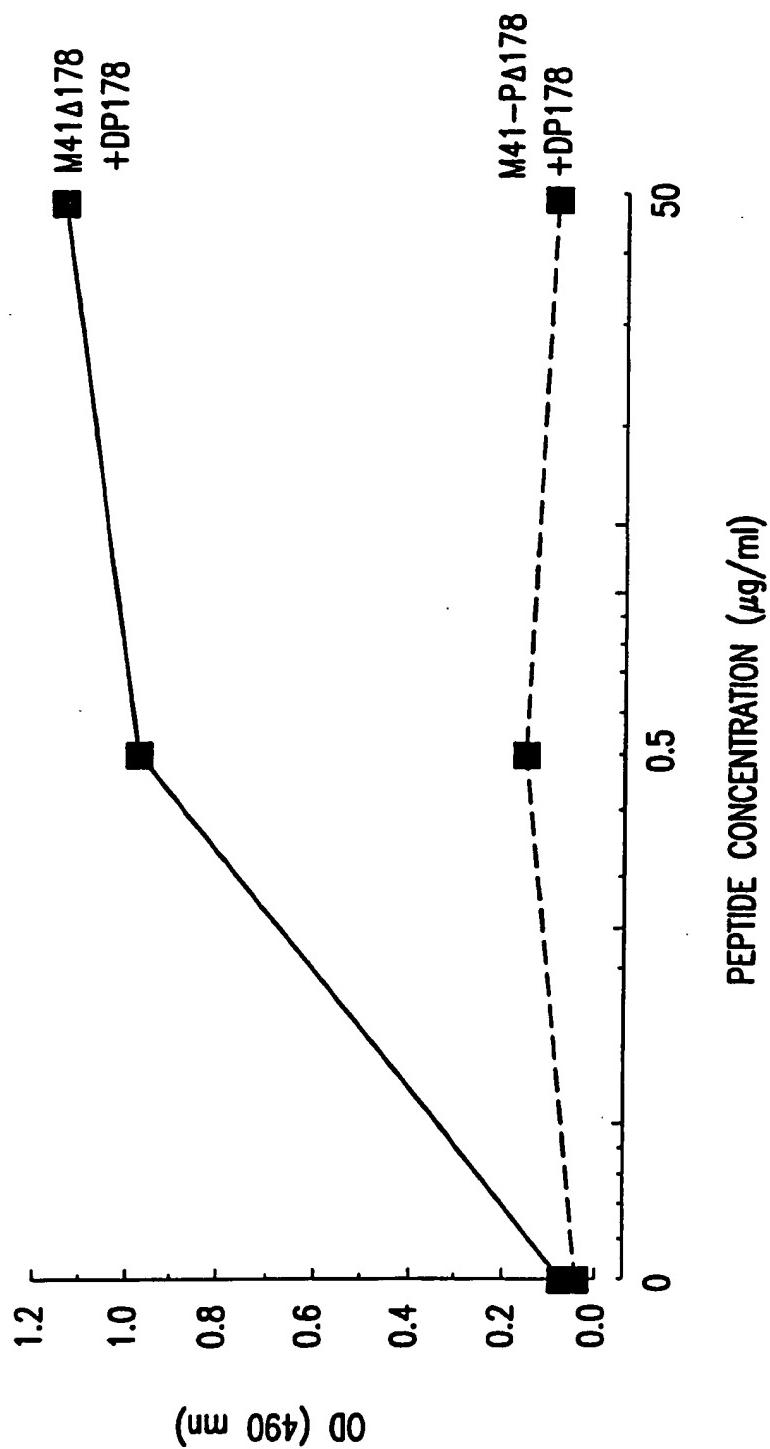


FIG. 10

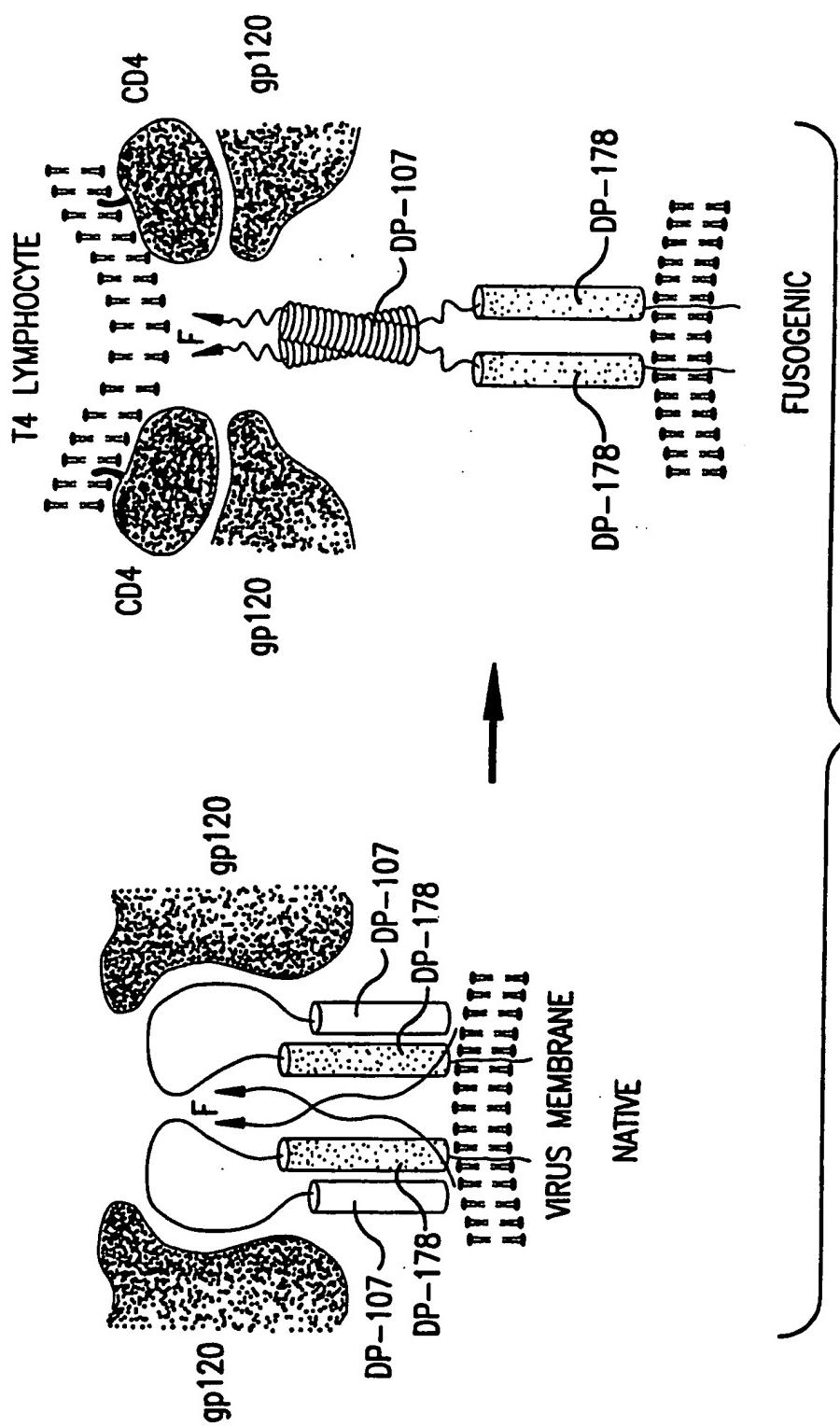


FIG. 11A

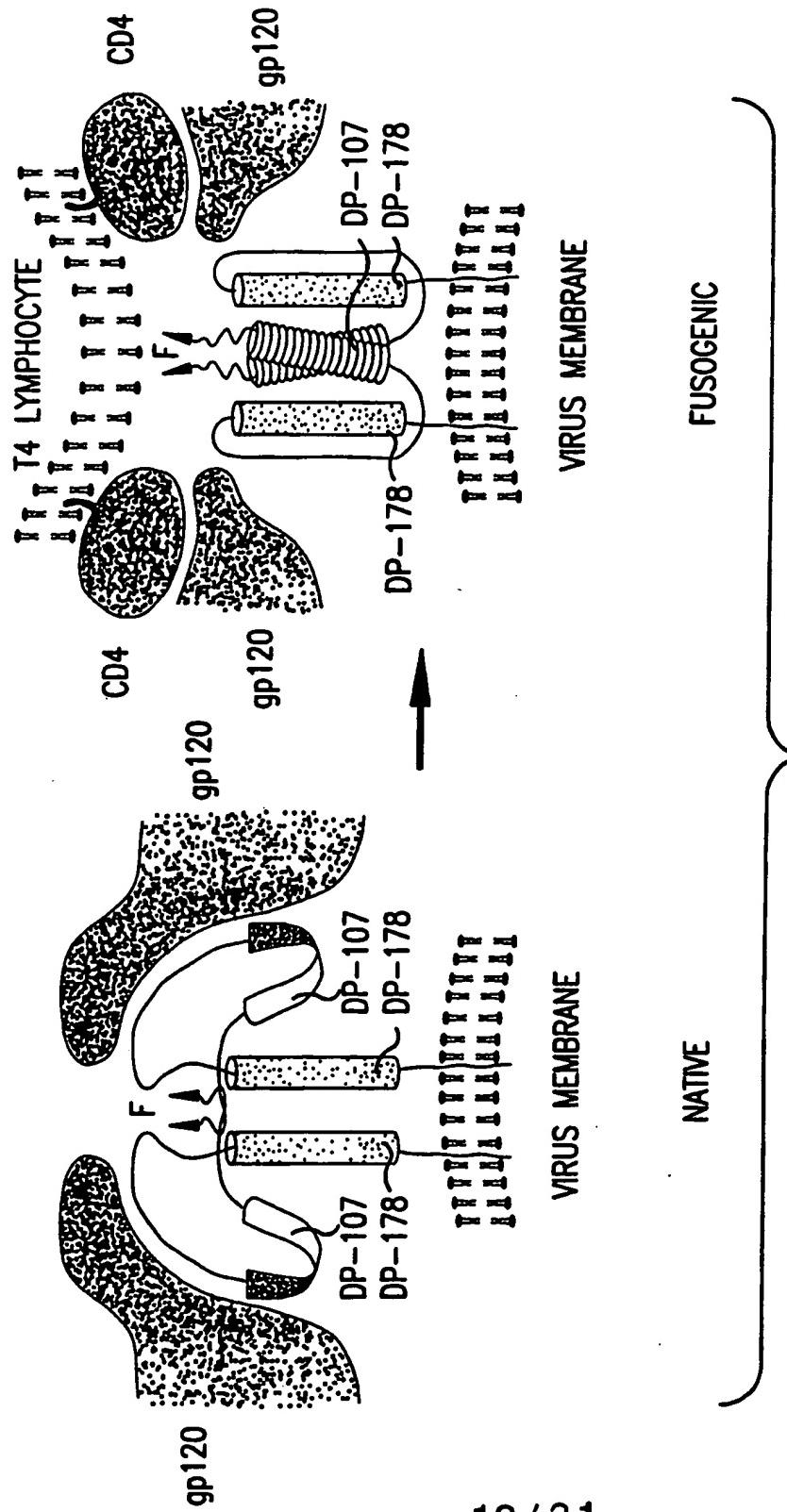


FIG. 11B

Sequence	Positions								Motifs
	A	D	A	D	A	D	A	D	
GCN4 (gcn4 yeast)	M K Q L E D K V	E E L L S K N Y H I	L E N E V A R L K K L	W {CFCIMPYW}					
C-FOS (fos human)	T D T L Q A E T D Q L E D E K S A L Q T E I A N L L K E	{CFGHIMPRWWY}							
C-JUN (c-jun human)	I A R L C E E K V K T L K A Q N S E L A S T A N M L R E Q	{AIIWV}							
C-MYC (myo human)	E Q K L I S E E D L L E K R R E Q L K H K L E Q L R N S	{CDFGHILPWWY}							
FLU LOOP 36	I E K T N E K F H Q I E K E F S E V E G R I Q D L E K Y	{ACFGMPWWY}							

FIG.12

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Sequence	Positions												Motifs					
	A	D	A	D	A	D	A	D	A	D	A	D						
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[ILQT] {CFIMPSTY}
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[ILQT] {CDFIMPST}
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[ILQT] {CDFIMPST}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[EKLNOV] {CDFKMPSVY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[EKLNOV] {CFKMPY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	L	Q	O	A	R	I	[EKLNOV] {CFKMPY}
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EKLOY] {ACFGMPRWY}
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EKLOY] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EKLOY] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EILNOV] {ACFGMPRWY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EILNOV] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	Q	E	K	N	E	[EILNOV] {CFGMPRVY}

FIG. 13

Sequence GCA4 (gcn4 yeast)	Positions				Parent Motif [LMNV] {CFGIMPW}	Hybrid Motif [ILMQTV] {CFIMPY}
	D	A	D	A		
DP-107 (env_hv1bru) L1=D	W K Q E D K Y E F L L S K N Y H I L E N E V A R I K K L				[ILQV] {CDF IMPST}	[ILMQTV] {CF IMPY}
DP-107 (env_hv1bru) L1=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[ILQV] {CDF IMPST}	[ILMQTV] {CF IMPY}
DP-107 (env_hv1bru) L1=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[ILQV] {CDF IMPST}	[ILMQTV] {CF IMPY}
DP-107 (env_hv1bru) L1=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[ILQV] {CDF IMPST}	[ILMQTV] {CF IMPY}
DP-107 (env_hv1bru) L2=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[EKL NOV] {CDF KAPSYY}	[EKLMQV] {CF IMP}
DP-107 (env_hv1bru) L2=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[EKL NOV] {CDF KAPS}	[EKLMQV] {CF IMP}
DP-107 (env_hv1bru) L2=D	N N L L R A E A Q Q H L L Q L T V W C K Q L Q A R I				[EKL NOV] {CDF KAPS}	[EKLMQV] {CF IMP}

FIG. 14

Sequence	Positions										Parent Motif	Hybrid Motif
	D	A	D	A	D	A	D	A	D	A		
GCK4 (gen4 yeast)	W K Q I F D K V E F I L S K N Y H I E N E V A R I L K K L	[LMNV]	{CFGIMPWY}									
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[EKLQY]	{ACFGMPRWY}	[EKLMDQY]	{ACFGMPWY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[EKLQWY]	{ACFGPRVY}	[EKLMDQWY]	{ACFGPRVY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[EFKLMQY]	{ACFGPRVY}	[EFKLMQWY]	{ACFGPRVY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[ELNQSY]	{ACFGMPRWY}	[ELNQSY]	{ACFGMPRWY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[ELNQSWY]	{ACFGMPRVY}	[ELNQSWY]	{ACFGMPRVY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[EFILNQSY]	{ACFGMPRWY}	[EFILNQSY]	{ACFGMPRWY}							
DP-178 (env_hv1bru)Y1=0	Y T S L I H S L I E E S O N Q Q E K N E Q E L L E D K	[EFILNQSWY]	{ACFGMPRVY}	[EFILNQSWY]	{ACFGMPRVY}							

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FIG. 16

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Sequence	Positions				Parent Motif	Hybrid Motif
	D	A	D	A		
GCN4 (gcn4 yeast)	M K Q L E D K V E F E L L S K N Y H L E N E V A R L K K L	[LMW]	[CFGIMPW]			
DP-107 (env_hv1bru) L=0	N N L L R A I E A Q H L L Q L T V W C I K Q L Q A R I L A V E R Y L K D Q	[LQV]	[CDFIMST]			
DP-178 (env_hv1bru) Y=0	Y T S L I H S L I E S Q N Q E Q K N E Q E L L E D K W A S L W N W F	[EFKQWY]	[CFGPRVY]			
GCN4 (gcn4 yeast)	M K Q L E D K V E F E L L S K N Y H L E N E V A R L K K L	[LMW]	[CFGIMPW]			
DP-107 (env_hv1bru) L=0	N N L L R A I E A Q H L L Q L T V W C I K Q L Q A R I L A V E R Y L K D Q	[LQV]	[CDFIMST]			
DP-178 (env_hv1bru) Y=0	Y T S L I H S L I E S Q N Q E Q K N E Q E L L E D K W A S L W N W F	[EFKQWY]	[CFGPRVY]			
GCN4 (gcn4 yeast)	M K Q L E D K V E F E L L S K N Y H L E N E V A R L K K L	[LMW]	[CFGIMPW]			
DP-107 (env_hv1bru) L=0	N N L L R A I E A Q H L L Q L T V W C I K Q L Q A R I L A V E R Y L K D Q	[LQV]	[CDFIMST]			
DP-178 (env_hv1bru) Y=0	Y T S L I H S L I E S Q N Q E Q K N E Q E L L E D K W A S L W N W F	[EFKQWY]	[CFGPRVY]			
GCN4 (gcn4 yeast)	M K Q L E D K V E F E L L S K N Y H L E N E V A R L K K L	[LMW]	[CFGIMPW]			
DP-107 (env_hv1bru) Y=0	Y T S L I H S L I E S Q N Q E Q K N E Q E L L E D K W A S L W N W F	[EFKQWY]	[CFGPRVY]			
GCN4 (gcn4 yeast)	M K Q L E D K V E F E L L S K N Y H L E N E V A R L K K L	[LMW]	[CFGIMPW]			
DP-107 (env_hv1bru) L=0	N N L L R A I E A Q H L L Q L T V W C I K Q L Q A R I L A V E R Y L K D Q	[LQV]	[CDFIMST]			
DP-178 (env_hv1bru) Y=0	Y T S L I H S L I E S Q N Q E Q K N E Q E L L E D K W A S L W N W F	[EFKQWY]	[CFGPRVY]			

FIG. 17

Sequence	Positions				Parent Motif	Hybrid Motif
	D	A	D	A		
LCN4 (gcn4 yeast)	M K Q L E D K V E E L L S K N Y H I L E N E	V A R L K K L	[LMWV] {CEGIMPYW}			
DP-107 (env_hv1bru) Y1=D	N N L L R A I E A Q Q H I L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[ILOV] {CQFIMPST}				
DP-107 (env_hv1bru) Y2=D	N N L L R A I E A Q Q H I L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[EKLNOV] {CFKAPS}				
DP-178 (env_hv1bru) Y1=A	Y T S L I H S L I E F S O N Q Q E K N E Q E L L E D K W A S L W N W F	[EFKLOWY] {FCFGAPRYY}				
DP-178 (env_hv1bru) Y1=D	Y T S L I H S L I E S Q N Q Q E K N E Q E L L E D K W A S L W N W F	[EFFLNSWY] {FCFGAPRWN}				
C-FDS (fso_human)	T D I L Q A E T D Q L E D E K S A L Q T E I A N L K E	[IKLT] {FCGHIPRWY}				
C-JUN (top1_human)	I A R L E E K V K I L K A Q N S E L A S T A N M L R Q	[AILW] {CQFGHILPWW}				
C-MYC (myo_human)	E Q K L I S E E D L L E K R R E Q L K H K L E Q L R N S	[ELR] {ACFGAPWY}				
SUBFLU LOOP 36	I E K T N E K F H Q I E K E F S E V E G R I Q D L E K Y	[FILT] {ACFLMPIYW} {CFP}				
					[AEFIKLMQQRSTWY] {CGCHP}	= {CGCHP} {CFP}

FIG. 18

P-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(1)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(2)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(3)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(4)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(5)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(6)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(7)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(8)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(9)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(10)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(11)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-X(1,12)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-X(13,23)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]

FIG. 19

Fusion Peptide **▼ALLMOTIS▼**
Peptide **▲107x178x4▲**
▼.....ELGFLG A AGSTMGARSM TLTVQARQ ▲LL SGIVQOO DP107-NNL

LRAIEAOOHLLOLTWVGKOLOARILAYER YLKDO-DP107 QLLG&♥ I WGC

♦107x178x4♦
♥ALLMOTIS♥ *LVS Coiled-Coil*
SGKLICT TAVP ♥WNASWS NKSLEQIWNN MTWM *E ♦WDRELNNN DP178-

~~XTSLIHSJ EESONOQEK NEOELLELDK*~~ WASLWNWE-DP178 NI

◆ Transmembrane Region ◆
TNWLWYIK♦ ◆ IFLIMIVGGLVGLRIVFAVLSIV NRVROGYS♥ PL

SFOTHLPTPR GPDR ♫P23LZIPC♪ ♫PEGIEE EGGERDRDRS IRLVNGSLAL IWDDLRSL♪ CL

♥ALLMOTIS♥ ♪107x178x4♪
F ♥SYHRLRDLL LIVTRIVELL GRRGW ♪EALKY WWWLLOXWSO

ELKNSAVSLL NAT♦ AIAVAEG TDRVIEVVQG A♥ CRAIRHPR

RIRQGLERIL L

FIG. 20

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Fusion **♥ALLMOT15♥**
 Peptide **▲107x178x4▲**
♥.....FLGEL LGVGSALAS GVA ▲VSKVLHL EGEVNKIKSA

P1&12LZIPC
LLSTNKAVVS LSNGVSVLTS KVLDLKNYID KQ♦♥ LL ♦PIVNKQ
▲107x178x4▲
SC ♦SISNIETV I♦ EFQQKNNRLLETREFSVNAG♦ VITTPVSTMLTNSELLSL

P1&12LZIPC
♥ALLMOT15♥
INDM ♦PI ♥TNDQ KKLMNSNNVQI V♦ RQQSYSI♦ MS IIKEEVLAYV

VQ♥ LPLYGVID TPCWKLHTSP LCTINTKEGS NICLRTDRG WYCDNAGSVS
 FFPQAETCKV QSNRVFCDTM NSLTPSEIN LCNVDIFNPK
 YDCKIMTSKT DVSSSVITSL GAIVSCYGKT KCTASNKNRG
 IIKTFNSNGCDYVSNKGMDTV SVGNTLYYVN KQEGKSLYVK G

P7, 12, & 23LZIPC
▲107x178x4▲ **♥ALLMOT15♥**
EPIINFYDPLVF ♦PSDE ♦EDASISQVNEKINOSLAF ♥I♦ RKSDELL♦

♦Transmembrane Region♦
HNVNA♦ GK STTN ♦IMITTLIVVIVILLS LIAVGLLLY♦ C♦

KARSTPVTLS KDQLSGINNI AFSN

FIG. 21

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Fusion
 Peptide ♦ALLMOTIS♦ ♦107x178x4♦
ELGFLG ♦AAGTA MGAAA ♦TALTYQSQHLLAGILOQQOKNLLAAV

♦107x178x4♦
EAQ♦ QQM ♦LKLTIWGVKNLNARVTALEKYLEDQARLN♦ AWG♦ CA

LVS Coiled-Coil
 ♦ALLMOTIS♦ ♦107x178x4♦
WKQVCHTTVP WQWNNRTPDW ♦NNMT *WLE ♦WERQISYLEGNTT

♦107x178x4♦
TQLEEARAQEEKNLD♦ AYQKLSS* WSDFWSW♦ FDF ♦SKWLN ♦ILK
 ♦ Transmembrane Region ♦
IGFLDVLGNGLRLLYTV♦ YS♦ CIARVRQGYS PLSPQIHIHP WKGQPDNAEG

PGEGGDKRKN SSEPWQKESG TAEWKSNWCK RLTNWCSISS IWLYNS

♦ALLMOTIS♦
 ♦CLTL LVHLRSAFQY IQYGLGELKA AAQEAVVALA RLAQNAGYQIWL♦

ACRSAYRA IINSPRRVRQ GLEGILN

FIG. 22

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Fusion Peptide **▼ALLMOTIS▼** **▲107x178x4▲**
**EAG** **▼VVL AGVALGVATA AQITAGLALHQ** ***LVS Coiled-Coil***
**EAG** **▼VVL AGVALGVATA AQITAGLALHQ** ***SNLNAQAIQ**

SLRTSLEQSNKAIEEIREATOETVIA* **VQGVQDY** ♦ VNNEL ♦ VP
♦ ALLMOTIS ♦
♦ 107x178x4 ♦
♦ P6 & 12LZIPC ♦
AMQHMSCELVGQRLGLRLLRYYTELLSIFGPSLRD ♦ **PISA** ♦ ♦ EISIOALIYAL

GGEHKILEKLGYSGSD ♠ MIALESRGIKTKI ♥ THVDLPGKF IILSISY

P1 & 12LZIPC
PTLSEVKGVIVHRLEAV SYNIGSQEWYTTVPRYIATNGYLISNFDESSCVFVS

ESAIQSQNSL YPMSPLLQQC IRGDTSSCAR TLVSGTMGNK FILSKGNVA

NCASILCKCY STSTINQSP DKLLTFLASD TCPLVEIDGA TIQVGGGRQYP

LVS Coiled-Coil
♥ALLMOTIS♥
♦P12 & 23LZIPC♦
DMVYEGKVAL G ♦PAISLD ♥RL *DVGTNLGNALKLDDAKVLI♦

◆ Transmembrane Region ◆
DSS+ NQILETVRSV* SFN ◆ FGSLL SVPILSCTAL ALLLIYCC ◆

K RRYQQTLKQH TKVDPAFKPD LTGTSKSYVR SL

FIG. 23

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Fusion ♥ALLMOTIS♥
 Peptide
 ♥.....FIGAI IGSVALGVA TAAQITAASA LIQANQNAAN ♣107x178x4♣
 ♣ILRLKESITA

TIEAVHEVTDGLSQLAVA♣ VG KM♥ QQFVNDQFNNTAQELDCIKITQQV

♥ALLMOTIS♥
 GVELNLYLTELTTV FGPQITSPAL ♥TQLTIQALYNAGGNMDYLLTKLGVG

♦P1 & 12LZIPC♦
 NNQLSSLIGSGLIT GN♥ ♦PILYDSQT QLLGIQVTLP SVGNLNNMRATYLET

LSVST TKGFASALVP KVVTQVGSVI EELDTSYCIE TDLDLYCTRI VTFPMSPGIY

SCLNGNTSAC MYSKTEGALT TPYMTLKGSV LANCKMTTCR CADPPGIISQ

♥ALLMOTIS♥
 ♣107x178x4♣
 NYGEAVSLID RHSCN ♣♥VLSLD GITLRLSGEF DATYQKNISI LDSQVIVTG

LVS Coiled-Coil
 *NLDISTELGNV NNSISNALDK LEESNSKLDK VNVKLSTSA ♦Trans-
 ♦LIT* XIA

membrane Region♦
LTAISLVCGILSLV♥♣ LACYLMY♦ KQKAQQKTLLWLGNNTLGQMRATTKM

FIG. 24

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Fusion **▼ALLMOTIS▼**
 Peptide **▲107x178x4▲ *LVS Coiled-Coil***
**FFGGV** **▲IG ▼TIALG *YATSAQITAAVALVEAKQARS DIEKLKE**

AIRDTNKAVQSVQSSIGNLIVAIKSVQ* DYVNKE▼▲ IVPSIARLGCEAAG

▼ALLMOTIS▼
▲107x178x4▲
LQLGIALTQH ▲▼YSELTNIEGDNIGSLOEKGIKLOGIASLYRTNITE▼▲

+P5 & 12LZIPC+
IFTTSTVDKYDIYDLLFTESIKVRVIDVDLNDYSITLQVRL +PLLTRLLNTQIYR

VDSISYNI+ QNREWYI+ PLPSHIMTKGAFLGGADVKECIEAFSSYIC

PSDPGFVLNHEMESCLSGNISQCPRTVVKS DIVPRYAFVNNGGVVANCITT

TCTCNGIGNRINQPPDQGVKIITHKECNTIGINGMLFNTNKEGT LAFYTP

▼ALLMOTIS▼
▲107x178x4▲
+P6 & 23LZIPC+
NDITLNNSVALD +PIDI +SIELN ▼KAKSDLEESKEWI+ RRSNOKL+

♦Transmembrane Region♦
DSIGNWHQSSTT ♦IIV♦ LIM IILEIINVTI II♦ ILAVKYY▼ R

IQKRN RVDQN DKPYVLTNK

FIG. 25

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Fusion

Peptide

.....GLFGAI AGFIENGWEGMIDGWYGFRHQNSEGTG

♦107x178x4♦

♥ALLMOTIS♥

LVS Coiled-Coil

*Q ♥AADLKST ♦QAAIDQINGKLNRYIEKTNEKEHQIEKEESEVEGRIQ

DLEKYVEDTKIDL* WSYNAELLVALENQHTI♦ DLT♥ DSEMNLKFKEKTR

RQLRENAEEMNGNGCFKIYHKCDNACIESIRNGTYDHDVYRDEALNNRFQIKG

VELKSGYKDWLWISFAISCFLLCVVLLGFIMWACQRGNIRCNICI

FIG. 26

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		RSV F2	YTSVITIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	CD	T-142	YTSVITIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
+	+/++	T-143	SVITIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
++	+/++	T-144	VITIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-145	ITIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-146	TIELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	-	T-147	IELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	-	T-148	ELSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	-	T-149	LSNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	-	T-150	SNIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	-	T-151	NIKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-152	IKENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-153	KENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-154	ENKCNGTDAYKL IKOELDKYKNAVTELQLLMQST
	+/-	T-155	

FIG.27

FIG. 28

AV	CD	HPF3	178	YTPNDITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT
-	-	189	YTPNDITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	190	PNDITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	191	NDITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	192	DITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	193	ITLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	194	TLNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	195	LNNNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	196	MNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	197	NNSVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	198	SVALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	199	VALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	200	ALDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	201	LDPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
+/-	+/-	202	DPIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
-	-	203	PIDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	204	IDISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	205	DISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	206	ISIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	207	SIELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	208	IELNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	209	EILNKA SKDLEE SKEWIRRNSNQKLDSIGNWHQSSTT	
++	++	210		

FIG. 29

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CD HPF3 107 GTIALGVATSAQITAVALVEAKQARSDIEKLKEAIRDTNKAQSVQSSIGNLIVAIKSVQDYVNKEIVP
 +/+ 157 ALGVATSAQITAVALVEAKQARSDIEKLKEAIRDT
 +/+ 158 LGVATSAQITAVALVEAKQARSDIEKLKEAIRDT
 +/- 159 GVATSAQITAVALVEAKQARSDIEKLKEAIRDTN
 +/+ 160 VATSAQITAVALVEAKQARSDIEKLKEAIRDTNK
 +/+ 161 ATSAQITAVALVEAKQARSDIEKLKEAIRDTNKA
 +/- 162 TSAQITAVALVEAKQARSDIEKLKEAIRDTNKA
 +/+ 163 SAQITAVALVEAKQARSDIEKLKEAIRDTNKAQ
 +/+++ 164 AQITAVALVEAKQARSDIEKLKEAIRDTNKAQSV
 +/+ 165 QITAVALVEAKQARSDIEKLKEAIRDTNKAQSV
 +/- 166 ITAAVALVEAKQARSDIEKLKEAIRDTNKAQSVQ
 +/- 167 TAAVALVEAKQARSDIEKLKEAIRDTNKAQSVQS
 +/- 168 AAVALVEAKQARSDIEKLKEAIRDTNKAQSVQSS
 +/- 169 AVALVEAKQARSDIEKLKEAIRDTNKAQSVQSSI
 +/- 170 VALVEAKQARSDIEKLKEAIRDTNKAQSVQSSIG
 +/- 171 ALVEAKQARSDIEKLKEAIRDTNKAQSVQSSIGN
 +/- 172 LVEAKQARSDIEKLKEAIRDTNKAQSVQSSIGNL
 +/- 173 VEAKQARSDIEKLKEAIRDTNKAQSVQSSIGNLIV
 +/++ 174 EAKQARSDIEKLKEAIRDTNKAQSVQSSIGNLIV
 T-40 AKQARSDIEKLKEAIRDTNKAQSVQSSIGNLIV
 +/++ 175 KQARSDIEKLKEAIRDTNKAQSVQSSIGNLIVAI
 +/+++ 176 QARSDIEKLKEAIRDTNKAQSVQSSIGNLIVAIK
 +/- 177 ARSDIEKLKEAIRDTNKAQSVQSSIGNLIVAIKS
 +/- 178 RSDIEKLKEAIRDTNKAQSVQSSIGNLIVAIKSV
 - 179 SDIEKLKEAIRDTNKAQSVQSSIGNLIVAIKSVQ
 - 180 DIEKLKEAIRDTNKAQSVQSSIGNLIVAIKSVQD
 - 181 IEKLKEAIRDTNKAQSVQSSIGNLIVAIKSVQDY
 - 182 EKLKEAIRDTNKAQSVQSSIGNLIVAIKSVQDYV
 +/++ 183 KLKEAIRDTNKAQSVQSSIGNLIVAIKSVQDYVN
 +/+++ 184 LKEAIRDTNKAQSVQSSIGNLIVAIKSVQDYVN
 - 185 KEAIRDTNKAQSVQSSIGNLIVAIKSVQDYVNKEIV
 - 186 EAIRDTNKAQSVQSSIGNLIVAIKSVQDYVNKEIV
 - 187 AIRDTNKAQSVQSSIGNLIVAIKSVQDYVNKEIV
 - 188 IRDTNKAQSVQSSIGNLIVAIKSVQDYVNKEIVP

FIG.30

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US94/05739

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : A61K 37/02, 39/12; C12Q 1/70; G01N 33/53

US CL : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, Biosis

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
NONE	NONE	NONE

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
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•	Special categories of cited documents:	"I"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Z"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
07 SEPTEMBER 1994	26 SEP 1994
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer JEFFREY STUCKER <i>J. Stucker</i>
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/US94/05739**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 2
because they relate to subject matter not required to be searched by this Authority, namely:
that the claimed subject matter is directed to mental processes.
2. Claims Nos.: 13-16 and 42-49
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
because the sequences have not been submitted to the International Searching Authority in electronic form.
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.